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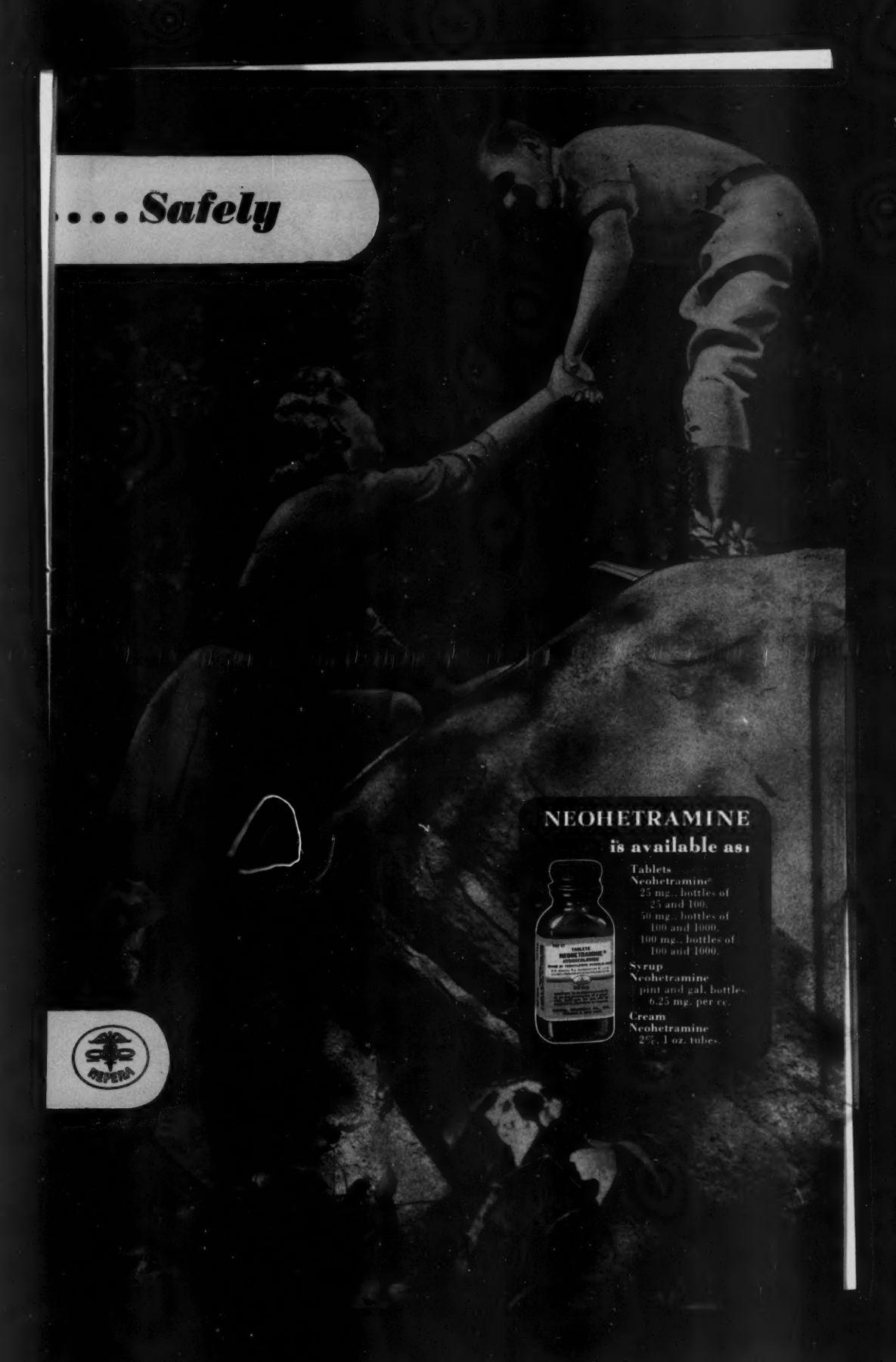
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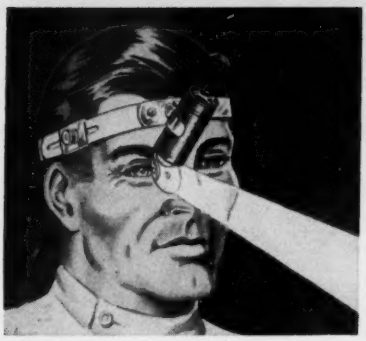

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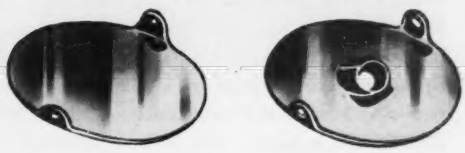

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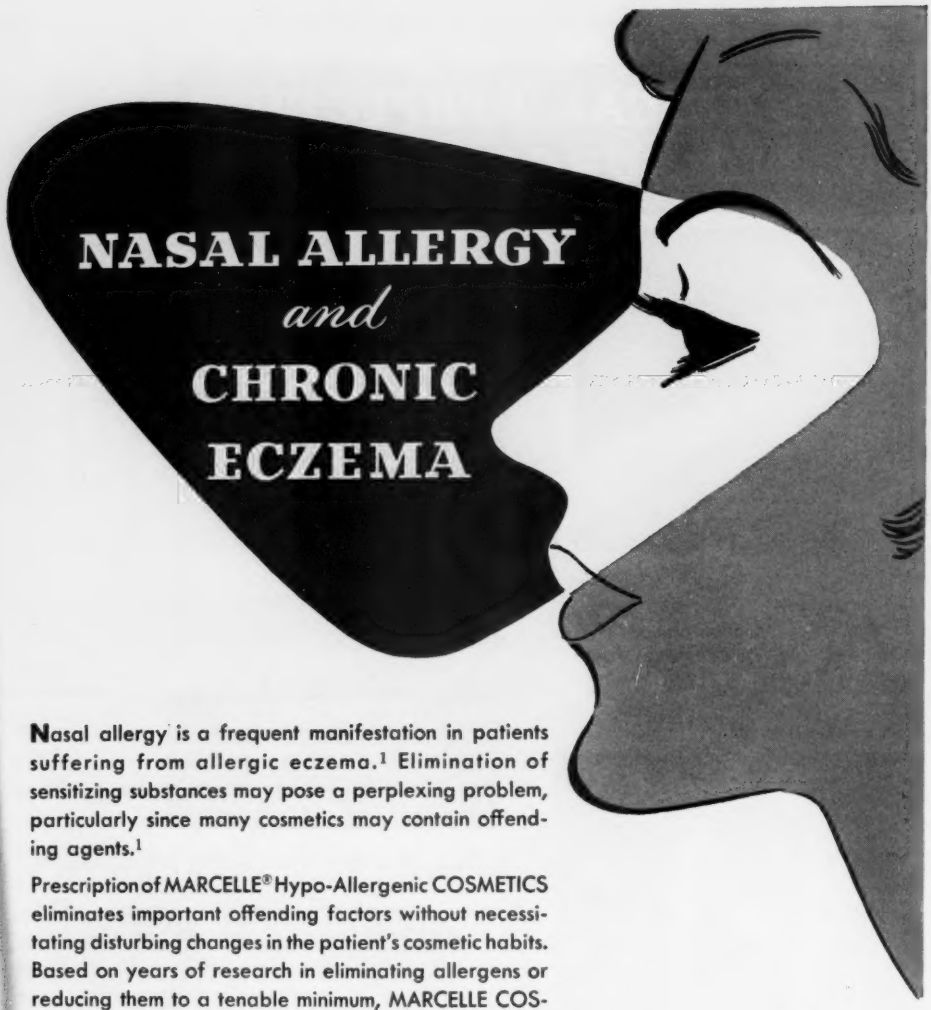

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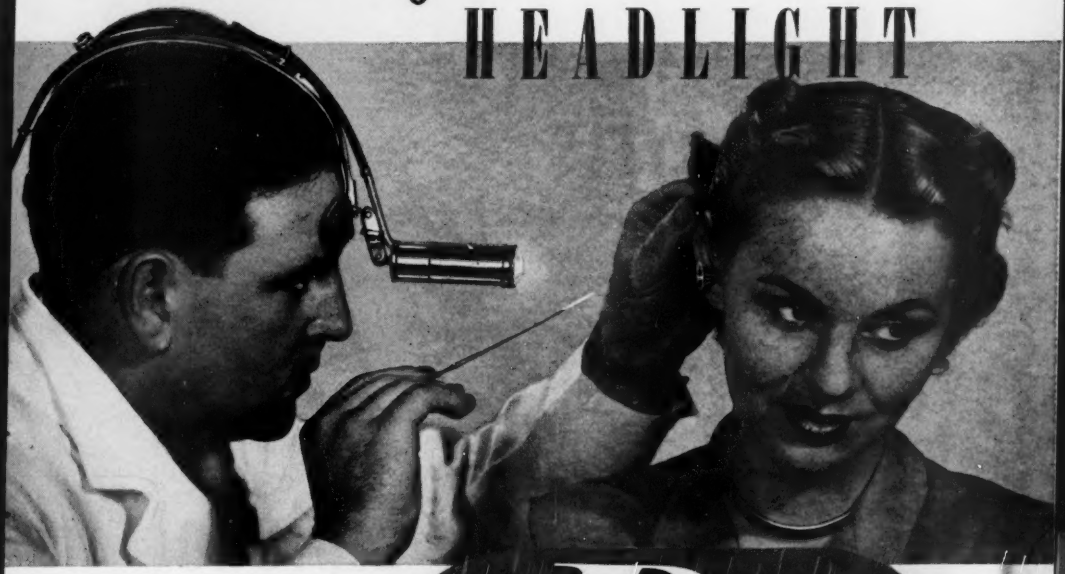

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VOLUME 53 MAY 1951 NUMBER 5

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DISTRIBUTION AND COMPARISON OF NASAL CILIA

G. EDWARD TREMBLE, M.D.
MONTREAL, CANADA

WHEN Leeuwenhoek made the first compound microscope, in Delft, Holland (Netherlands), about 1675, he opened up an entirely new field of anatomical study. Until that time, histology was a closed book and all observations were made on gross specimens. Anton de Heide, another Dutchman, noted cilia for the first time in 1683, and 12 years later Leeuwenhoek described ciliary movement. Nearly 150 years later Sharpey [1] (1830) observed ciliary motion in the sinuses and trachea of dogs, and in 1834 Purkinje and Valentin [2] discovered ciliated epithelium on the oviductal walls of certain vertebrates. For nearly 60 years no mention of cilia or their movement was made in the literature. Toward the end of the last century a number of articles appeared,[3] and, as a result, there has been renewed interest in the physiology of cilia.

In many animals, bodily movements depend on muscular activity and ciliary action is limited to mucous membrane surfaces. Often the safety of an animal depends on fleetness of foot, and, in such a case, movement of the cilia, though important, is of secondary consideration. In minute invertebrates which move about slowly in the water, cilia are of paramount importance and not muscle fibers. Certain sea urchins and molluscs are covered with highly specialized cilia which aid in the ingestion of food as well as in locomotion.

For convenience, a cilium might be described as a permanent hairlike projection, with a to-and-fro movement, on the surface of a cell which contains a nucleus.

Ciliary movement is the work which a cell does by means of multiple cilia. Functioning constantly, this action in no way appears to alter the size or outline of the cell.

According to Gray,[4] "the simplest type of vibratile organ is the flagellum which is characteristic of flagellate Protozoa and of sponges. Each flagellum is a separate

---

Presented before the Cleveland Otolaryngologic Society, Cleveland, Dec. 6, 1950.

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3. (*a*) Schäfer, E. A.: On the Structure of Amœboid Protoplasm, with a Comparison Between the Nature of the Contractile Process in Amœboid Cells and in Muscular Tissue, and a Suggestion Regarding the Mechanism of Ciliary Action, Proc. Roy. Soc., London **49**:193-198, 1891. (*b*) Bronn, H. G.: Klassen und Ordnungen, des Their-Reichs, wissenschaftlich dargestellt in Wort und Bild, edited by O. Bütschli, Leipzig, C. F. Winter, 1887, pt. 3. (*c*) Saguchi, S.: Studies on Ciliated Cells, J. Morphol. **29**:217-279, 1917.

4. Gray, J.: Ciliary Movement, Cambridge Comparative Physiology, New York, The Macmillan Company, 1928.

vibratile unit with its own blepharoplast [5] and it is usually of considerable length. As a rule one cell or individual protozoan does not possess more than four flagella. When a cell possesses numerous vibratile units these are usually much shorter than typical flagella and they are more commonly known as cilia."

When we move up the scale in the animal kingdom, we find ciliated cells have become more highly specialized. As an example, the gills of filibranch molluscs, such as Mytilus edulis, provide suitable material for study. The ciliated epithelium of these marine animals shows a more striking resemblance to human respiratory mucous membrane than the classic example of the epithelium on the roof of a frog's mouth. Two points of difference stand out at once. The frontal cilium of Mytilus is longer than human nasal cilium (about 12 microns, the diameter of a polymorphonuclear cell, as compared to 7 microns—about the diameter of a red blood corpuscle), and its effective beat describes an arc of 180 degrees in contrast to a stroke of perhaps 100 to 120 degrees by human nasal cilium.

However, in many respects the cells with their attached cilia are alike, although in the light of our present knowledge it is unwise to carry the comparison too far.

The laterofrontal cells of Mytilus are tall columnar ciliated cells which rest on a chitinous supporting structure resembling a basement membrane. An endothelial layer in which are blood cells and blood spaces lies below this.

Fig. 1.—Drawing of Euglena (after Dellinger). The intracellular rootlets of the fibrils form the long flexible flagella.

In a longitudinal view the cells are rectangular, the average width of the cells being 2.6 microns. The distal end of the cell is slightly wider than the proximal. The nucleus of the laterofrontal cell has the shape of a compressed oval which lies with its long axis parallel with the long axis of the cell. It averages 8.6 microns in length in Mytilus edulis and lies within the lower one half to two thirds of the cell. In fixed and stained preparations, the nucleus has a stronger affinity for basic dyes than do the other cells of the gill. The basophilic substance of the nucleus is in the form of granules which are irregularly distributed.[6] Clear cytoplasm, interspersed throughout with granules, fills the cell. Perhaps the most important structures in the cytoplasm, apart from the nucleus, are the ciliary rootlets, which appear to have their origin in the basal bodies just proximal to the cuticular border on the surface. These rootlets, which seem like threads, can be traced downward in stained specimens but become indistinct and finally lost in the protoplasm around the nucleus. Whether or not they are definitely connected with the cilia in the basal bodies is not known.

5. "A flagellum consists of an axial filament (axoneme) and a thin sheath of cytoplasm. The axoneme itself takes its origin in a minute granule, the blepharoplast, which is situated in the cytoplasm, and sometimes upon the surface of the nuclear membrane. The axoneme passes to the surface of the body and there acquiring a thin sheath of cytoplasm, becomes the flagellum."—Alexeieff, A.: Sur les cercomonadine intestinales de Calliphora erythrocephale mg. et de Lucilia sp., Compt. rend. Soc. Biol. **71**:379-382, 1911.

6. Lucas, A. M.: Regulation of Ciliary Activity, J. Morphol. **51**:147-193, 1931.

The cilia, as shown in the diagram, number 20 to 30 to each cell. They appear to originate in the basal bodies on the proximal side of the cuticular membrane and extend up through the surface. There is still a marked difference of opinion as to what is the exciting cause of ciliary movement. This, of course, has been mentioned frequently.

A number of investigators, such as Grave and Schmitt,[7] Carter [8] and Copeland,[9] have found evidence suggesting that the nervous system exerts some influence on ciliary movement. Grave and Schmitt described a series of fibers in ciliated cells of the lamellibranch gill which they consider might control the movement of the cilia. McDonald, Leisure and Lenneman [10] noted that electrical and chemical stimulation of the sympathetic fibers which innervate the ciliated epithelium lining of the frog's pharynx causes the cilia to beat rapidly, and that stimulation of parasympathetic fibers causes the cilia to beat slowly. Others, such as Parker [11] and

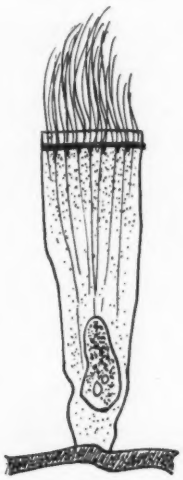

Fig. 2.—Cross section of laterofrontal epithelial cell from Mytilus gill.

Lucas,[6] believe that the activating and controlling mechanism is an inherent property of ciliated epithelium. Parker expressed himself very definitely when he stated (p. 65),

> The fact . . . that no one has ever been able to control ciliary activity through nerves and all the cases of ciliary coordination thus far brought forward can be explained on the basis

7. Grave, C., and Schmitt, F. O.: A Mechanism for the Coordination and Regulation of Ciliary Movement as Revealed by Microdissection and Cytological Studies of Ciliated Cells in Mollusks, J. Morphol. **40**:479-515, 1925.

8. Carter, G. S.: On the Nervous Control of the Velar Cilia of the Nudibranch Veliger, Brit. J. Exper. Biol. **4**:1-26, 1926-1927.

9. Copeland, M.: Ciliary and Muscular Locomotion in the Gastropod Genus Polinices, Biol. Bull. **42**:132-142, 1922.

10. McDonald, J. F.; Leisure, C. E., and Lenneman, E. E.: New Principles in the Control of the Activity of Ciliated Epithelium, Tr. Am. Acad. Ophth. **33**:318-354, 1928.

11. Parker, G. H.: The Elementary Nervous System, Philadelphia, J. B. Lippincott Company, 1919.

of neuroid (nerve-like) transmission, renders the belief in the nervous control of cilia very improbable. In fact, it may be stated that at present there is not the least ground for the assumption that true nervous activity is in any direct way involved in ordinary ciliary reactions.

He also mentioned later:

These impulses pass through the deeper protoplasmic parts of the tissue and call forth the successive activity of the cilia which thus gives evidence of this transmission wave.

Lucas stimulated the branchial nerve of Mytilus with an electrical current but failed to produce any visible effect upon the activity of the cilia. Evidence as presented in the present investigation points to the conclusion that the impulse regulating ciliary activity of the lamellibranch gill is not dependent upon the nervous system for its transmission.

Therefore coordination and regulation of ciliary activity probably lie within the ciliated epithelium itself, and consideration of certain facts observed concerning the wave movement of cilia may be suggestive on the basis of Parker's theory of neuroid transmission.

A year later Lucas [12] was perhaps somewhat more definite. Using Modiolus gill as an example, he stated,

Each ciliated cell is, therefore, a nerve-muscle-like complex and somewhere between the two there probably exists a neuromuscular type of junction. The basal body which is connected with the end of the cilium, and which is in contact with the cell surface, may prove to be the locus of this junction.

Although the exact mechanism of ciliary movement is uncertain, and this applies to human nasal cilia as well, a few established facts stand out. It has been proved beyond all doubt that the motility of a cilium does not depend on the cell structure as a whole to which it is attached. Peter,[13] in 1899, was the first to demonstrate that even when a ciliated protozoan was crushed into small pieces, the cilia continued to beat as long as they were connected organically with a fragment of cytoplasm. More recently, Erhard,[14] and Gray [15] have shown that marked destructive changes can occur in the proximal cytoplasm, including the nucleus, without interfering with ciliary movement. In view of these findings, it is generally agreed that the motive stimulation of the cilia lies in the distal portion of the cell—that is, just below the surface. Nothing further is known at the present time.

Clinically, this concept was later verified by Hilding [16] when he described his investigations of the common cold. Nasal swabs taken in the first two days of a cold often show individual cast-off surface cells or fragments of cells with their attached clumps of cilia still beating vigorously.

In the human embryo, nasal cilia develop early from the three germinal layers—ectoderm, mesoderm, and entoderm.[17] They appear at the fourth month of fetal life, about the time the tonsil and internal ear make their appearance. Shortly after birth, nasal cilia seem identical under the microscope with those of adults. Motion pictures of cilia, taken at various speeds and age periods, show the frequency and

12. Lucas, A. M.: Coordination of Ciliary Movement: Effect of Temperature upon Ciliary Wave Length, J. Morphol. **53**:265-276, 1932.

13. Peter, K.: Das Centrum für die Flimmer- und Geisselbewegung, Anat. Anz. **15**:271-283, 1898-1899.

14. Erhard, H.: Studien über Flimmerzellen, Arch. Zellforsch. **4**:309-442, 1910.

15. Gray, J.: The Mechanism of Ciliary Movement: Photographic and Stroboscopic Analysis of Ciliary Movement, Proc. Roy. Soc., London, s. B **107**:313-332, 1930.

16. Hilding, A.: The Common Cold, Arch. Otolaryng. **12**:133-150 (Aug.) 1930.

17. Gray, J.[4]

amplitude of the beat to be similar. Slow motion pictures, at 64 frames a second instead of the usual 16, do not appear to show any change in the rate of movement.

Human cilia are resistant and powerful structures, which often keep on beating many hours after death. According to Proetz,[18] they have two very important qualities. Active ciliary movement almost always exists within a sinus, even in the presence of severe infection with thick pus, and after removal of the mucous membrane lining of a sinus regeneration takes place in about five months, with normal-appearing mucous membrane complete with active cilia. As mentioned, human cilia are about 5 to 7 microns in length, although they vary slightly in different areas. They are just under 0.3 micron in diameter, and the distance between them is about equal to their own diameter. Although Lucas[19] found 8.5 cilia on a cell surface 6.2 microns in diameter, this estimate seems too conservative. Highly magnified photomicrographs show 20 to 30 cilia to a cell and this also appears to be borne

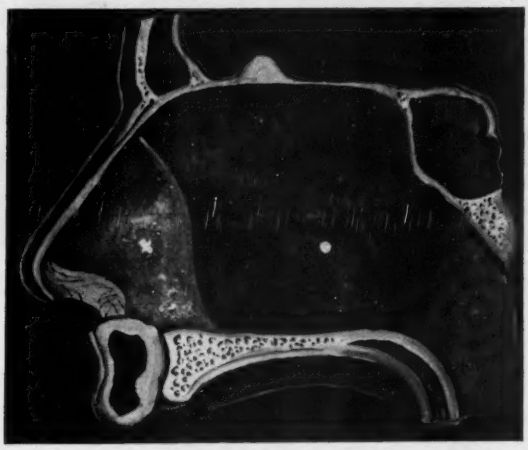

Fig. 3.—Septum showing roughly one third inactive area and two thirds (darker area) active.

out in motion pictures of nasal mucosa. The effective stroke occupies about one quarter of the time of the recovery stroke, and there are about 250 to 300 complete cycles a minute.

Except for a few areas, the whole of the respiratory tract is lined with ciliated epithelium. In the adult, the anterior third of the septum and lateral wall, the olfactory area, the pharynx and the edges of the vocal cords are devoid of cilia.

Nasal mucous membrane varies in thickness, often being several millimeters deep over the inferior and middle turbinates and parts of the septum. In other areas, such as the sinuses, it frequently is less than a millimeter thick.

Generally speaking, the exposed anterior third of the septum and lateral wall gives an appearance of heaped-up cells resembling squamous epithelium with large

18. Proetz, A. W.: Studies of Nasal Cilia in the Living Mammal, Ann. Otol., Rhinol. & Laryng. **42**:778-788, 1933.

19. Lucas, A., in Cowdry, E. V.: Special Cytology: The Form and Functions of the Cell in Health and Disease, ed. 2, New York, Paul B. Hoeber, Inc., 1932, p. 409.

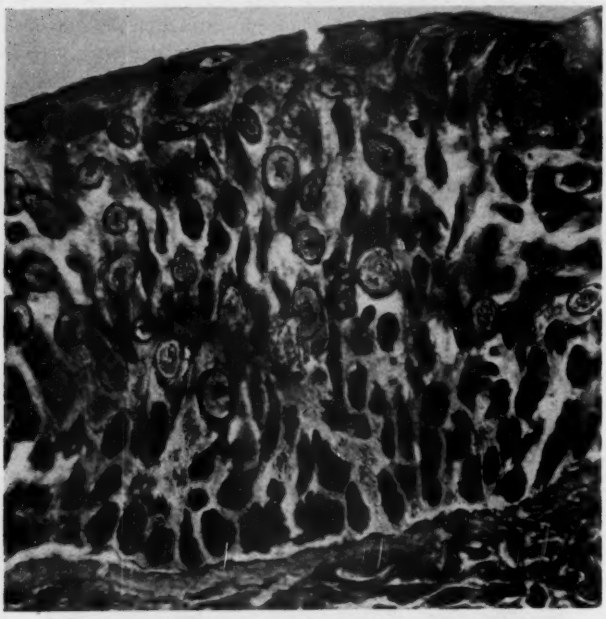

Fig. 4.—Section of membrane from anterior third of septum (area marked by cross in figure 3) showing absence of cilia on the surface.

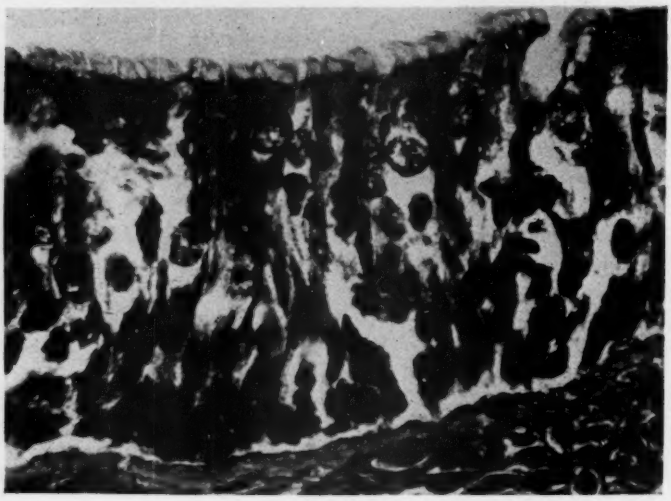

Fig. 5.—Photomicrograph of posterior active area (marked by dot in figure 3). Short well developed cilia are present, interspersed with mucous and serous glands.

oval nuclei and no cilia. The cells are often 10 to 15 layers in depth, and the basement membrane is usually quite distinct. On the posterior two thirds of the septum the character of the mucous membrane changes. The stroma shows a tremendous

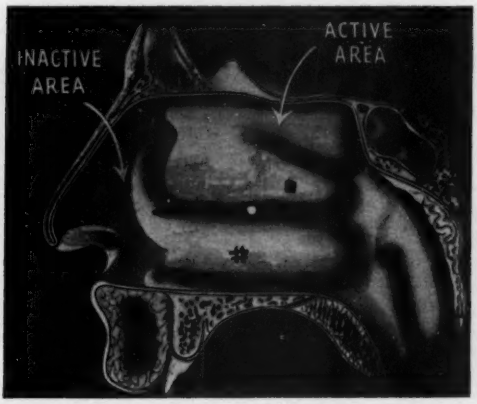

Fig. 6.—Lateral wall, showing anterior nonciliated area and posterior ciliated surface.

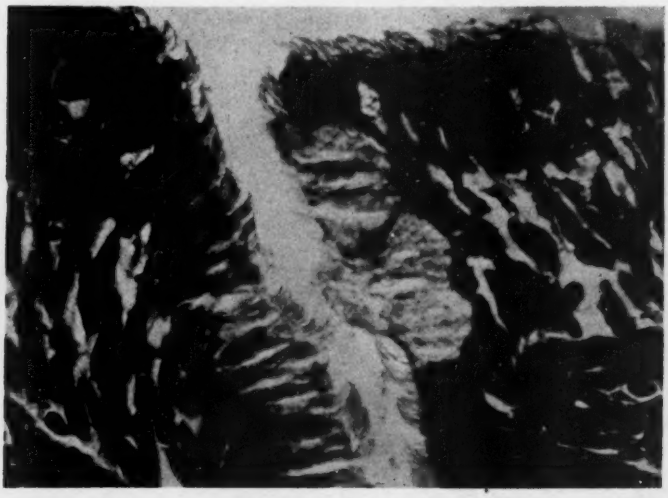

Fig. 7.—Toward the posterior tip of the middle turbinate (marked by square dot in figure 6) mucus-secreting tubular and racemose glands are found. Well developed cilia are present.

number of mucus-secreting and serous glands with marked lymphocytic infiltration. The mucosa is thicker in some areas, such as the tubercle and lower part of the septum, and much thinner in others. There is usually a very definite basement membrane superimposed with eight or 10 irregular layers of high columnar cells.

As shown in figure 5, the cilia in a typical area appear short in comparison with the length of the surface cells. The irregular grouping of the cilia may be due partly to the fixing and staining of the slide.

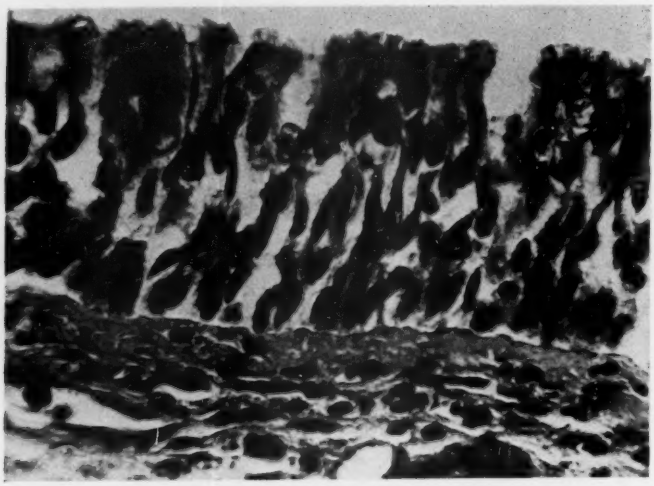

Fig. 8.—Section of middle third of inferior turbinate (marked by crosshatch in figure 6) showing high columnar surface cells superimposed by relatively short cilia.

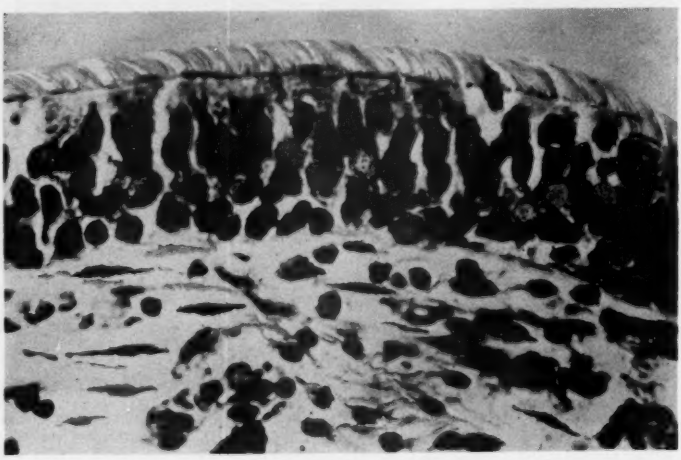

Fig. 9.—Section from middle meatus (marked by dot in figure 6) showing short columnar cells. The cilia on the surface are long and well developed to carry the increased load.

Over the lateral wall anteriorly the blasts of inspired air soon change the typical respiratory mucous membrane to a low cuboidal or squamous form of epithelium.

This applies to the anterior end of the middle and inferior turbinates as well, and the microscopic picture is similar to that described above for the anterior portion of the septum.

The mucosa of the middle third of the turbinates resembles that on the corresponding surface of the septum with pseudostratified, deep, columnar cells surmounted with relatively short, irregular cilia. Below these are six to eight layers of replacement cells on a well marked basement membrane. Over the superior turbinates the cilia are, as a rule, poorly developed.

Toward the posterior tip of the middle and superior turbinates the stroma is richly supplied with glands. In contrast, the stroma of the inferior turbinate contains many large cavernous spaces and relatively few glands. Protected regions, such as the middle and inferior meatuses, have a thinner type of mucosa, which consists of four or five irregular layers of replacement cells lying on a basement membrane. The surface epithelium contains short columnar cells with long powerful cilia. The cilia are perhaps better developed here than anywhere else in the nose and their movement is well coordinated.

SUMMARY

An attempt has been made in this résumé to correlate some of the known facts of ciliary movement in certain lower forms of animal life with those facts known about ciliary movement in humans. The marked variations in normal human nasal mucosa and submucosa in different areas and the distribution of cilia are described.

In general, it may be stated that the thickness of nasal mucous membrane is dependent on the degree of impact and air flow over the surface. For instance, the exposed inactive anterior third of the septum and lateral wall has a thick membrane of 10 to 15 cells in depth, while the membrane in the active posterior two thirds has a layer of only eight to 10 cells. In protected areas not influenced by direct air currents, such as the middle and inferior meatuses, the cells are four or five layers deep, and the membrane is thinnest of all in the sinuses, where the exchange of air is negligible. The mucosal lining of the sinuses consists of only two or three layers of short cuboidal cells and is often only a fraction of a millimeter in thickness. Except for the ethmoid cells, the stroma is loosely attached to the sinuses.

In other words, the more exposure to outside air laden with dust, smoke and fumes of all kinds, the thicker the epithelium; the less exposure to these influences, the thinner the membrane. The depth of the stroma containing the blood vessels is in proportion to the depth of the epithelial layer. The stroma is widest in the exposed anterior portion of the nose and disappears almost entirely in the sinuses.

The references given are not intended to cover the subject completely in any way. A recent article by Ballenger [20] gives a very comprehensive view and a much more complete bibliography of the literature on ciliary activity.

1390 Sherbrooke Street West.

20. Ballenger, J. J.: A Study of Ciliary Activity in the Respiratory Tract of Animals, Ann. Otol., Rhin. & Laryng. **58**:351-369, 1949.

UNCOMMON CONDITIONS IN THE FIELD OF OTOLARYNGOLOGY SEEN IN OFFICE PRACTICE

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KINSTON, N. C.

THE PERIOD covered by this publication ranges from Aug. 1, 1946 to Jan. 1, 1948 (Goldsboro, N. C.) and from Feb. 1, 1948 to Aug. 1, 1950 (Kinston, N. C.). During this time a number of pathological conditions which were unusual by virtue of their inherent nature, location, or both were encountered in the office practice of otolaryngology, and it is believed that they are of sufficient interest to warrant recording.

In the preparation of this abstract it was necessary to delete from the original thesis a considerable portion of the content and bibliography and to reduce the number of case reports and illustrations. Routine laboratory tests made on all hospitalized patients consisted of a complete blood count, urinalysis, and blood Wassermann test, but detailed results of the laboratory examinations have for the most part been omitted.

I. TUMORS

Angiolipoma of the Larynx

A case of laryngeal angiolipoma was not found recorded in the literature from 1903 through 1948. New and Erich [1] did not find a case of this type in a total of 722 cases of patients with benign laryngeal growths examined at the Mayo Clinic over a period of 30 years, and the authors particularly stressed the rare occurrence of true vascular tumors of the larynx.

Case 1.—H. A. W., a white man, aged 68 years, referred by Dr. Donnie H. Jones Jr., was seen in the office for the first time Feb. 17, 1947. The patient was unable to talk because of a severe obstructive laryngeal dyspnea, and his son volunteered the following information: About ten days previously an unaccustomed hoarseness developed, and on the night of February 12 the patient experienced two brief paroxysms of coughing associated with the expectoration of a moderate amount of bright red blood on each occasion. After this attack difficulty in breathing developed and gradually progressed in severity until the patient sought medical attention. On February 15 he experienced difficulty in swallowing, and two days later there was an exacerbation of all symptoms.

Presented in part before the Fifty-Fifth Annual Meeting of the Seaboard Medical Association of Virginia and North Carolina, Dec. 7, 1950, Elizabeth City, N. C.

The pathological studies were made by Drs. R. P. Morehead and C. C. Carpenter, Department of Pathology, Bowman Gray School of Medicine, Winston-Salem, N. C.

Abridgment of a thesis accepted by the Faculty of the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania, in partial fulfillment of the requirements for the degree of Master of Medical Sciences (M.Sc. [Med.]) for graduate work in Otolaryngology.

1. New, G. B., and Erich, J. B.: Benign Tumors of the Larynx: A Study of 722 Cases, Arch. Otolaryng. **28**:841-910 (Dec.) 1938.

Examination of the ears, nose, and throat disclosed nothing remarkable except for the laryngeal findings. Mirror laryngoscopy revealed the presence of a large mass which almost filled the laryngeal introitus. The growth was covered by a yellowish cheeselike granular material and moved slightly on respiration. The tumor was attached to the right side of the larynx, but the exact site of origin was not determined. There were no palpable cervical lymph nodes.

The patient was hospitalized, and an emergency tracheotomy was done. Intramuscular penicillin therapy was instituted and continued throughout the entire period of hospitalization. The general physical examination revealed the presence of a generalized arteriosclerosis and a blood pressure of 160/90. Results of routine laboratory studies were found to be within normal limits, and a chest roentgenogram was reported by Dr. C. E. Howard to show essentially normal conditions.

One week after the patient's admission to the hospital direct laryngoscopy was attempted but abandoned because of brief but profuse hemorrhage from the larynx. Thyrotomy under local anesthesia was then performed. The laryngeal tumor was found to be a large firm yellowish growth partially covered with fresh blood clot, and it was attached by a small base to the laryngeal surface of the right aryepiglottic fold near the lateral margin of the epiglottis. It was dissected free from its attachment, and the site of origin was cauterized with the actual current. There was no undue bleeding. The postoperative course was uneventful, and the patient was discharged from the hospital March 10, 1947.

Pathologist's Report.—Gross Description: The specimen consisted of a large irregular mass which measured 2.5 by 2 by 1.75 cm. Externally, it was made up in part of a finely granular glistening grayish brown tissue and in part of a friable discolored material. Upon being sectioned, the large mass of tissue was found to be moderately soft, light grayish white near its periphery, and discolored in its central portion. The tissue was homogeneous throughout.

Microscopic Description: The sections showed that the surface of the tumor was partially covered with a thin layer of squamous epithelium which was well differentiated. The epithelial covering was in part ulcerated, with necrosis extending into the underlying tissue. The tumor was composed of endothelium-lined spaces containing blood. In addition, there were numerous polygonal-shaped cells which in some areas appeared to be differentiating into fat cells. Larger blood vascular spaces were seen which were lined by endothelium and which possessed a well defined wall. Fat stains made with scarlet red revealed the presence of numerous globules of fat. The final diagnosis was angiolipoma with chronic inflammation and ulceration.

Follow-Up Observations.—The patient was last seen in October, 1948, at which time there was no evidence of recurrence of the tumor or residual hoarseness following operation. Dr. W. L. Thompson did a nephrectomy on the patient in June, 1948, and the pathological diagnosis was clear cell carcinoma of the kidney. The patient died in January 1950.

Comment.—This rare benign vascular tumor of the larynx attained a large size before it produced symptoms, representing a classic example of how completely the laryngeal introitus may be gradually obstructed before symptoms are produced. The possibility of spontaneous hemorrhage of appreciable degree from this type of growth must be considered.

Mixed Tumors of the Cheek

Mixed tumors of the salivary gland type are rarely encountered in the cheek. A tabulation of several large series of cases reported in the literature gave a total of 2,609 mixed tumors found in different anatomical locations, and of this number only 40 occurred in the cheek.[2] This is an incidence of 1.5 per cent. Even though

2. (*a*) McDonald, J. R., and Havens, F. Z.: A Study of Malignant Tumors of Glandular Nature Found in the Nose, Throat and Mouth, S. Clin. North America **28**:1087-1106 (Aug.) 1948. (*b*) Ash, J. E.: Mixed Tumors of the Salivary Gland Type: Preliminary Report, Am. J. Orthodontics (Oral Surg. Sect.) **33**:522-531 (July) 1947. (*c*) Payne, R. T.; Tod, M. C.,

(Footnote continued on next page)

this survey does not represent a complete review of the literature on this subject, it does afford an approximate concept of the frequency of mixed tumors in the cheek area. Additional single case reports of mixed tumors of the cheek were recorded in recent years by Thoma, Howe, and Wenig [3]; Solero [4]; Jame and Sohier [5]; Berard, Creyssel, and Soustelle [6]; Snellman,[7] and Theissing.[8]

Hellwig [9] recently summarized the theories concerned in explaining the histogenesis of mixed tumors and discussed his own concept that they arise from remnants of the notochord. Ash,[2b] however, found Hellwig's idea of a notochordal origin untenable for several reasons. Morehead,[10] after his study of several personal cases of cutaneous mixed tumors and a review of the literature on this subject, concluded that mixed tumors of the skin, salivary glands, and breast are similar morphologically, and that they may arise from the ectoderm.

McFarland's histological classification of mixed tumors was recently modified by Ash,[2b] and Dockerty and Mayo [11] removed cylindromas from the general category of mixed tumors because of their tendency to infiltrate, recur, and metastasize. They considered these growths in the light of adenocarcinomas of the cylindroma type. Stewart, Foote, and Becker [12] further clarified the histopathologic picture of salivary gland tumors by separating out of this group the so-called mucoepidermoid

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and Lederman, M.: The Diagnosis, Classification, and Treatment of Tumors of the Salivary Glands: Symposium, Brit. J. Radiol. **17**:3-12 (Jan.) 1944. (*d*) Robbins, G. F.: Tumors of Salivary Gland Origin, Surgery **14**:924-930 (Dec.) 1943. (*e*) Sheldon, W. H.: So-Called Mixed Tumors of the Salivary Glands, Arch. Path. **35**:1-20 (Jan.) 1943. (*f*) McFarland, J.: The Histopathologic Prognosis of Salivary Gland Mixed Tumors, Am. J. M. Sc. **203**:502-519 (April) 1942. (*g*) Stones, H. M.: Mixed Tumors of the Mouth, Brit. Dent. J. **69**:77-86 (Aug. 1) 1940. (*h*) Blady, J. V., and Hocker, A. F.: Sialography: Its Technique and Application in the Roentgen Study of Neoplasms of the Parotid Gland, Surg., Gynec. & Obst. **67**:777-787 (Dec.) 1938. (*i*) Ruppe, C.: Acquisitions récentes sur les épithéliomas et les tumeurs de la cavité buccale, Presse méd. **46**:350-354 (March 5) 1938. (*j*) Chen, H. I., and Loucks, H. H.: Composite Tumors of the Salivary Glands: A Clinico-Pathologic Study of 45 Cases, Chinese M. J. **47**:138-153 (Feb.) 1933. (*k*) Noosten, H. H., and Vos, J. J. T.: Parabuccal Mixed Tumors with Special Consideration of Cylindromas of Antrum of Highmore, Geneesk. tijdschr. Nederl.-Indië **73**:1453-1476 (Nov. 7) 1933.

3. Thoma, K. H.; Howe, H. D., and Wenig, M.: Tumors of the Mouth and Jaws, Am. J. Orthodontics (Oral Surg. Sect.) **31**:260-288 (April) 1945.

4. Solero, C.: Submucosal Mixed Tumor of the Cheek: Case, Minerva Med. **2**:134-138 (Aug. 18) 1942.

5. Jame, L., and Sohier, A.: Tumeur mixte de la joue, Bull. Soc. franç. dermat. et syph. **42**:463-468 (March) 1935.

6. Bérard, Creyssel and Soustelle, J.: Tumeur mixte salivaire dégénérée de la muqueuse jugale, à type histologique de cylindrome, Lyon chir. **32**:381-383 (May-June) 1935.

7. Snellman, A.: Beiträge zur Kenntnis der Morphologie und Morphogenie der sog. Mischgeschwülste der grossen Speicheldrüsen mit besonderer Berückstchtigung der epithelialen Zellelemente derselben, Arb. path. Inst. Univ. Helsingfors **6**:243-366, 1931.

8. Theissing, G.: Ein Mischtumor der Wange: Ein Beitrag zur Pathologie und Pathogenese der Mischtumoren, Ztschr. Laryng., Rhin. **19**:353-358, 1929-1930.

9. Hellwig, C. A.: Mixed Tumors of the Salivary Glands, Arch. Path. **40**:1-10 (July) 1945.

10. Morehead, R. P.: Mixed Tumors of the Skin, Arch. Path. **40**:107-113 (Aug.) 1945.

11. Dockerty, M. B., and Mayo, C. W.: "Cylindroma" (Adenocarcinoma, Cylindroma Type), Surgery **13**:416-422 (March) 1943.

12. Stewart, F. W.; Foote, F. W., and Becker, W. F.: Muco-Epidermoid Tumors of Salivary Glands, Ann. Surg. **122**:820-844 (Nov.) 1945.

growths arising from the salivary gland ducts. Hempleman and Womack [13] presented a summary of the essential features of the varied and complex histology of mixed tumors, and by means of special staining technique they demonstrated the presence of both mesenchymal and epithelial mucus in these growths. McFarland [2f] emphasized the futility of the histopathologic prognosis of salivary gland mixed tumor with the simple statement that "at present our methods are no more accurate or scientific than the flipping of a coin."

Mixed tumors are found most frequently in the major salivary glands of persons between the ages of 20 and 40 years, affect the sexes equally, show no predilection for right or left side, and are rare in the Negro race. Heinecke [14] observed a mixed tumor of the parotid gland in a newborn child. Slow growth is characteristic, the average time between discovery of the tumor and operation being seven to eight years as reported by Robbins,[2d] McFarland,[15] and Wood.[16] The growths vary in size, and the usually movable and sessile primary growths may occasionally be fixed or pedunculated. After operative removal, mixed tumors recur in 20 to 45 per cent of patients, as reported by several authors. Recurrent tumors show the histopathological features of the original growth, but they may exhibit infiltrative tendencies. Metastasis to the regional lymph nodes, lungs, and pleura occurs occasionally and is most likely to take place in the recurrent growths.

Mixed tumors of the cheek appear as painless slow growing lumps or swellings, which are responsible for varying degrees of difficulty in speech, mastication, deglutition, and respiration. Large tumors of the cheek or palatal region may cause pressure erosion of the adjacent bony structures and involvement of the surrounding soft tissues, including large nerves. Ulceration may develop in extensive growths of long duration, and infection, followed by death from terminal aspiration pneumonia, occurs.

The diagnosis of mixed tumors is made from the clinical examination of the growths, laboratory findings, and x-ray studies, including sialography as advocated by Blady and Hocker.[2h] It is doubtful that biopsy is indicated if one can be reasonably certain of the diagnosis on clinical grounds. A ruptured capsule resulting from biopsy may be a factor in the recurrence of the growths, and the microscopic examination of small pieces of tissue is not always satisfactory.

Enucleation is probably the method of choice in the treatment of mixed tumors of the cheek, but enucleation may be combined with excision in some cases. McFarland [17] emphasized the futility of attempting to treat mixed tumors with x-ray and radium, stating that this method has only palliative value at best. He also advised against removing small growths, since recurrence is more likely to follow. Many authors, however, advocate removal as soon as the diagnosis is made, irrespective of the size of the growth.

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13. Hempleman, L. H., and Womack, N. A.: The Pathogenesis of Mixed Tumors of the Salivary Gland Type, Ann. Surg. **116**:34-42 (July) 1942.

14. Heinecke, cited by Brunschwig, A.: Mixed Tumor of the Tongue and Sublingual Gland, Surg., Gynec. & Obst. **50**:407-415 (Feb.) 1930.

15. McFarland, J.: Ninety Tumors of the Parotid Region, Am. J. M. Sc. **172**:804-848 (Dec.) 1926.

16. Wood, F. C.: The Mixed Tumors of the Salivary Glands, Ann. Surg. **39**:57-97 and 207-239 (Jan.) 1904.

17. McFarland, J.: The Treatment of Mixed Tumors of the Salivary Glands by Roentgen Rays and Radium, Am. J. Roentgenol. **46**:506-517 (Oct.) 1941.

Case 2.—R. L. J., a white man, aged 56 years, referred by Dr. J. L. Harrell, was seen in the office for the first time Sept. 3, 1946. The patient complained of a painful swelling in the left cheek and difficulty in opening his mouth. In 1943, while shaving, he accidentally discovered a small painless lump in his left cheek, but there was no increase in size until one year later, when gradual enlargement was noted. Later, while eating, he discovered the presence of "lumps" in the left side of his mouth. About Aug. 1, 1946, the mass in the left cheek began to enlarge rapidly and became painful. Three days prior to the patient's being seen in the office, there was a rapid exacerbation of all his symptoms, and he was forced to seek medical attention.

Examination of the ears, nose, and throat disclosed nothing remarkable except for the tumefaction in the left cheek region and a moderate degree of trismus. Palpation of the mass externally revealed that it was exquisitely tender, smooth, firm, and slightly movable. There was no fixation of the overlying skin, and the mass did not transmit light. It was found that the tumor had an extensive origin from the upper half of the buccal mucosa of the left cheek, being surrounded, however, by varying amounts of grossly normal mucous membrane. The involved mucosa had a wrinkled appearance, was firm to palpation, and presented a yellowish appearance anteriorly, with a purplish red color posteriorly, suggesting a chronic inflammatory state. The orifice of the left parotid duct was not identified. A few nontender lymph nodes

Fig. 1 (case 2).—Mixed tumor removed from the left cheek.

were palpated in the anterior cervical chain bilaterally. The chest roentgenogram revealed normal conditions, and sinus roentgenograms revealed some clouding of the left antrum without evidence of bone destruction.

A diagnosis of mixed tumor was not entertained at this time, and the patient was hospitalized for biopsy under local anesthesia. The pathologist rendered a tentative diagnosis of mixed tumor on the basis of the biopsy specimen. The general physical examination and routine laboratory studies disclosed conditions within normal limits on this admission.

The patient was readmitted to the hospital Sept. 23, 1946, and the tumor was removed under local anesthesia preceded by heavy preoperative sedation. An external approach through the skin of the left cheek was employed. The pathological buccal mucosa along with the hopelessly enmeshed terminal parotid duct was extirpated, a free margin of grossly normal tissue surrounding the growth being obtained. The stump of the parotid duct was left free in the operative cavity. Penicillin was administered intramuscularly throughout the entire uneventful postoperative period, the patient being discharged from the hospital two weeks later. The only complication of the operation was an injury to the mandibular branch of the facial nerve.

Pathologist's Report.—Gross Description (fig. 1): The specimen of tissue measured 5.5 by 3 by 2.5 cm. and was irregular in outline. One side appeared to be covered by wrinkled grayish white epithelium, while the rest of the tumor, though partially encapsulated, was roughened and grayish brown. The cut surface showed most of the tissue to be a dense grayish white with some brownish mottling at one end. The consistency was rather firm throughout.

Microscopic Description: Sections through this tissue showed one small area of apparently normal salivary gland made up of two types of acini. One type showed large pale-staining cells with very small basal nuclei, while the other type showed almost a cuboidal epithelium. Near this area, and extending through the rest of the tumor mass, were small glands and large sheets of cells with fairly large hypochromatic nuclei and variable amounts of cytoplasm. These cells were uniform in size, shape, and staining characteristics. One section showed well differentiated stratified squamous epithelium with the tumor cells coming just beneath the epithelium proper. The large sheets of cells were broken into tiny lobules by thin fibrous septums, and there was attempted gland formation in most of the lobules. Hyalinization was present, and in the center of the tumor there was a large amount of necrosis. The tumor showed invasive tendencies and would have been classified by some as an "invading adenoma." The pathologist was of the opinion, however, that the tumor arose from embryonic ectodermal cells of the type ordinarily encountered in mixed tumors of the salivary glands. The final diagnosis was mixed tumor of the salivary gland type with features of a cylindroma.

Postoperative Course.—The mandibular branch of the facial nerve recovered its function in about four weeks following operation. The patient was last seen Aug. 12, 1950, at which time there was no evidence of recurrence of the tumor.

Comment.—In this case one may postulate a source of origin from the small salivary glands of the buccal mucosa, the embryonic ectodermal tissues of the cheek, or perhaps from Stensen's duct. The cylindromatous features of this tumor place it in the category of a potentially malignant neoplasm.

II. CYSTS AND FISTULAS

Cysts of the Floor of the Mouth: Ranulas

Many types of cystic swellings in the floor of the mouth have been referred to as ranulas. For this reason statistical data were of limited value in establishing a definite incidence for these growths, opinions were divergent regarding their etiology, and histopathological studies of ranulas were found to be limited and somewhat conflicting in nature. In like manner, the clinical features and symptoms recorded in descriptions of individual or group case reports of ranulas varied in accordance with the types of swelling considered by the individual authors to be examples of these growths. Many phases of the problem of ranulas were adequately discussed by Baker,[18] Morf,[19] Halstead,[20] Thompson,[21] Goldman,[22] Cottalorda,[23] Stein,[24] Fitzwilliams,[25] Tsuzuki,[26] Ferreira,[27] and Johnston.[28]

18. Baker, W. M.: On Ranula, St. Barth. Hosp. Rep. **7**:134-141, 1871.

19. Morf, P. F.: A Study of Ranula, Surg., Gynec. & Obst. **1**:505-511 (Dec.) 1905.

20. Halstead, A. E.: Three Cases Illustrating Points in the Surgical Pathology of the Region of the Embryonic Branchial Clefts, S. Clin., Chicago **1**:323-333 (April) 1917.

21. Thompson, J. E.: The Relationship Between Ranula and Branchio-Genetic Cysts, Ann. Surg. **72**:164-170 (Aug.) 1920.

22. Goldman, J.: Contribution à l'étude du traitement de la grenouillette sublinguale par la marsupialization, Thesis, Paris, 1922.

23. Cottalorda, M.-J.: Contribution à l'étude de la pathogénie de la grenouillette sublinguale commune, Ann. anat. path. **1**:441-468 (July) 1924.

24. Stein, O. J.: Cysts in the Floor of the Mouth, Ann. Otol., Rhin. & Laryng. **34**:1028-1041 (Dec.) 1925.

25. Fitzwilliams, D. C. L.: Ranula, Brit. J. Surg. **14**:472-485 (Jan.) 1927.

26. Tsuzuki, M.: Ranula and Syphilis, Am. J. Surg. **37**:127-131 (July) 1937.

27. Ferreira, C.: Sobre o tratamento da ranula, Rev. méd. Paraná **9**:199-205 (July-Aug.) 1940.

28. Johnston, W. H.: Cysts of the Floor of the Mouth, Ann. Otol., Rhin. & Laryng. **51**:917-930 (Dec.) 1942.

Chronic ranulas, or "blue-domed cysts," typically occur as small benign thin-walled cystic swellings in the sublingual area that are soft and fluctuant, painless, and blue to violet in color. They are usually unilateral and unilocular. Ordinarily, they lie above the mylohyoid muscle, but they may project around the posterior border of this structure and cause a cystic swelling in the submaxillary region of the neck. The contents consist of a viscid fluid that can be distinguished from saliva by chemical tests. These growths are most frequently found in persons in the middle years of life and occur with equal frequency in the male and female. They rarely attain a large size, and acute infections are uncommon complications. Spontaneous rupture with prompt recurrence is not unusual. Chronic ranulas develop slowly with a sense of the presence of a foreign body as the chief complaint. If there is cervical extension, the patient also notes the presence of a mass in the neck.

The diagnosis of ranulas is made from the history and observations on clinical examination, x-ray studies, and microscopic examination of the cyst walls.

Chronic ranulas have been treated by incision and drainage, aspiration and injection of irritating chemicals, and by surgical procedures calculated to produce permanent fistulization into the floor of the mouth. None of these methods produce uniformly good results. Ferreira [27] used surgical diathermy successfully in the treatment of eight patients with ranulas and recommended the method as a simple, rapid, bloodless, and efficient office procedure. The method of choice in the treatment of chronic ranulas is total extirpation by either the oral or the submental approach, or a combined approach when this can be accomplished.

CASE 3.—L. A. M., a white girl, aged 14 years, referred by Dr. Lee Overman, a dentist, was seen in the office for the first time April 3, 1948. She stated that approximately one month previously she had awakened one morning conscious of a painless swelling in the left side of the floor of the mouth. The area was swabbed with an antiseptic on two separate occasions, without benefit. During the ensuing two weeks, there was an occasional discharge of "pus" from the swollen area, with a temporary decrease in the size of the mass. On one occasion during this time a painless swelling developed in the left side of the neck and disappeared within 24 hours without recurring. The patient consulted her dentist about the possibility of a dental connection.

Examination of the ears, nose, and throat disclosed essentially normal conditions. In the left sublingual area somewhat medial and anterior to the sublingual gland was a soft unilocular light blue cystic mass, which measured approximately 2.5 cm. in length. It was smooth, nontender, and movable, transmitted light, and did not pit on pressure. The dome of the cyst contacted the under surface of the tongue but did not displace this structure. No mass was palpated in the neck; saliva was seen to flow from the left submaxillary duct, and a probe was introduced into the duct for some distance without difficulty. The left sublingual gland appeared to be grossly normal. A diagnosis of cyst in the floor of the mouth was made and removal advised.

The patient was hospitalized April 7. The general physical examination disclosed conditions essentially normal, and the results of routine laboratory studies were within normal limits. Operation was performed on the day of admission with 1 per cent procaine hydrochloride anesthesia. Because of adhesions to the surrounding soft tissues, the cyst ruptured before the dissection was completed. The remainder of the sac wall was removed by sharp dissection, and the cavity was allowed to remain open. The patient was discharged from the hospital the following day, and intramuscular penicillin therapy was given during the postoperative period, which was uneventful.

The findings at operation showed that the cystic mass was pear shaped, the tapered portion being near the apparent source of origin in the depths of the floor of the mouth. The left submaxillary duct was grossly normal. Bartholin's duct was not identified, and there was no

obvious connection between the cyst and the sublingual gland, which appeared to be normal. The contents of the cyst were a clear, viscid, yellowish, and odorless fluid.

Pathologist's Report.—Gross Description: The specimen consisted of several ragged fragments of brownish gray material amounting to less than 1 cc. Most of the fragments were membranous and stringy in character.

Microscopic Description: These fragments appeared to be portions of a thin-walled cyst. The wall was fibrous and showed a chronic inflammatory reaction. One surface of one of the fragments was covered by a layer of stratified squamous epithelium. The diagnosis was chronically inflamed cyst wall compatible with ranula.

Follow-Up Observations.—The patient was last seen Sept. 3, 1949, at which time there was no recurrence of the cyst.

Acute Cystlike Dilatation of the Submaxillary Duct

Two cases of acute cystlike dilatation of the right submaxillary duct were observed and are presented because of their unique clinical features.

Case 4.—P. E., a white man, aged 49 years, was first seen in the office on the night of Oct. 9, 1948. He stated that about 2 o'clock on the same afternoon he suddenly became conscious of an annoying dryness on the right side of his mouth which was not relieved by drinking water. About two hours later pain developed below the right jaw, and he then became aware of a slight swelling in this area. The pain soon disappeared, but the swelling persisted. At supper that night the neck swelling suddenly increased in size, but there was no accompanying pain. The patient sought medical attention because of the swelling.

Examination of the ears, nose, and throat disclosed essentially normal conditions except for a depressed scar over the right frontal region and scarring of the right ethmoidal area due to an old traumatic injury and subsequent operative intervention. The patient wore ill-fitting artificial dentures, and when these were removed it was seen that the terminal portion of the right submaxillary duct was moderately edematous, with petechial hemorrhages in this area. Along the course of the duct was an almond-shaped swelling, which measured about 2.5 cm. in length. The overlying mucosa appeared to be normal; the bulge was tender to palpation, and its presence was unknown to the patient. No calculus was palpated. The right submaxillary gland was moderately enlarged and tender to palpation.

The sublingual swelling was gently massaged, and after a brief interval a foreign body the size, shape, and color of a cantaloupe seed was suddenly expelled from the duct, followed by a gush of cloudy fluid and disappearance of the sublingual swelling. Massage of the right submaxillary gland resulted in the expulsion of a similar but smaller type of foreign body from Wharton's duct, with a discharge of fluid that grossly resembled saliva. There was some decrease in the size of the submaxillary gland. The foreign material disintegrated easily when compressed, and there was nothing to suggest minute calculi.

The following day the submaxillary swelling was slight, there was no sublingual swelling, and again there was no clinical evidence of a calculus. The patient refused x-ray studies. Four days later the edema and hemorrhages of the duct region had disappeared. The patient was last contacted in August 1949, at which time he reported that there had been no recurrence of symptoms.

Case 5.—J. W. O., a white man, aged 29 years, referred by Dr. J. L. Dupree Jr., a dentist, was first observed in the office March 22, 1949. The patient stated that three days previously he experienced soreness and burning under the right side of his tongue and shortly afterward became conscious of a swelling in this area and in the right side of his neck. The swellings increased in size and became slightly more painful at meal time. Seven months previously he had experienced a similar episode, which had lasted about 24 hours.

Examination of the ears, nose, and throat disclosed nothing remarkable except for a deviated nasal septum. Inspection of the right sublingual area revealed the presence of a reddish almond-shaped swelling, measuring about 2.5 cm. in length, along the course of the right submaxillary duct. The mass was tender to palpation, and a small whitish particle was seen protruding from the orifice of Wharton's duct. The right submaxillary gland was slightly enlarged and tender to palpation. Roentgenograms were reported as not revealing the presence of a calculus. After roentgenograms were made, the sublingual swelling was massaged, with the

resultant expulsion of several large pieces of jelly-like material followed by cloudy fluid. There was prompt disappearance of the sublingual mass, but this area remained a deep red color. Massage of the right submaxillary gland resulted in the escape of a cloudy fluid from the duct, and the gland returned to normal size.

The following day, there were no swellings and the floor of the mouth presented a normal color. Palpation, however, revealed the presence of a small calculus in the middle third of Wharton's duct (fig. 2). The calculus was removed in the office with 1 per cent procaine hydrochloride anesthesia, and the postoperative course was uneventful. The patient was last seen Aug. 8, 1950, at which time he stated that he still remained free of symptoms, and no abnormalities were noted.

Attempts by the pathologist to section the foreign material failed. Examination under the microscope revealed that it was composed of desquamated epithelial cells, degenerated cells, and white blood cells.

Comment.—Case 3 represents an example of the generally accepted concept of chronic ranulas, and the probable site of origin was the sublingual salivary or mucous glands. The swelling in the left submaxillary region which developed for one day and then disappeared was probably due to compression of Wharton's duct by a temporary enlargement of the cyst in the floor of the mouth. It is considered that the cyst was successfully treated by total extirpation.

The difficulty in case 4 most likely resulted from trauma to the submaxillary duct by the ill-fitting dentures and its occlusion by inspissated debris. The larger

Fig. 2 (case 5).—Calculus and debris removed from the right submaxillary duct.

mass of the latter provided complete obstruction to the egress of saliva, while the smaller mass in the middle of the duct caused only a partial obstruction to the lumen. In this manner, saliva was permitted to accumulate in the intervening portion of the duct between the foreign bodies, with resulting cystlike dilatation of the duct wall. The same mechanism of obstruction existed in case 5, and this case demonstrates most emphatically that one should not minimize the clinical examination of a salivary gland duct when roentgenograms fail to reveal the presence of a calculus.

Cysts of the Epiglottis

Cysts of the epiglottis are relatively rare. Beschorner,[29] in 1877, found 14 cases of epiglottic cysts in a total of 693 cases of laryngeal polyps collected from the literature. Pursiegle [30] reviewed all cases of tumors of the epiglottis reported prior to 1905 and found that 40 per cent of the growths were cysts. Glas [31] reported a personal experience with seven cases of epiglottic cysts out of a total of 16 cases of cysts of the larynx, and Jackson and Coates [32] stated that they had observed 35

29. Beschorner: Über Epiglottis-Cysten, Berlin klin. Wchnschr. **14**:620-621, 1877.

30. Pursiegle, J. B.: Étude sur les tumeurs de l'épiglotte, Thesis, Lyon, no. 83, 1905.

31. Glas, E.: Über Larynxcysten, Arch. Laryng. u. Rhin. **19**:285-305, 1906-1907.

32. Jackson, C., and Coates, G. M.: The Nose, Throat, and Ear and Their Diseases, Philadelphia, W. B. Saunders Company, 1929, p. 901.

cases of laryngeal cysts, in 23 of which the lesions sprang from the epiglottis. Kallay [33] found 24 cases of epiglottic cysts out of a total of 46 cases of laryngeal cysts published in the literature during the 15 year period prior to 1942. New and Erich,[1] at Mayo Clinic, found 35 cysts in a total of 722 benign neoplasms of the larynx, and four were located on the epiglottis.

Epiglottic cysts are generally classified as (1) retention or mucous; (2) blood (hemorrhagic) or lymph; (3) embryonal or congenital, and (4) implantation. Retention cysts are most frequently encountered. They usually develop as a result of an inflammatory reaction in the duct or periductal region of a mucous gland, but their formation has been attributed to the mechanical blockage of the excretory ducts of mucous glands,[34] and to trauma incident to labor.[35] Chiari [36] stated that blood or lymph cysts arise from distention of the blood or lymph vessels or from serous effusions into the connective tissue spaces. Kahler [37] and Glas [31] agreed that embryonal cysts arise from an epithelial germ that becomes kinked off during a faulty union of the bilateral anlage of the epiglottis, but Kahler conceded the possibility that they might arise from the branchiogenic system as advocated by Louys.[38] Glas [31] reported the only case of implantation cyst of the epiglottis found in the literature.

Epiglottic cysts of the retention type are usually lined by columnar or cuboidal glandular epithelium [39] or stratified columnar or squamous epithelium.[40] Hemorrhagic cysts are usually enclosed by a wall of fibrous tissue without epithelial lining.[39] Kahler's [37] embryonal epiglottic cyst and Glas's implantation cyst of the epiglottis were both lined internally and externally by stratified pavement epithelium. Jackson and Jackson [41] recorded an epiglottic cyst considered by the pathologist to have arisen from aberrant tonsillar tissue, the occluded crypt of which formed the inner lining of the cyst.

Cysts of the epiglottis can occur anywhere from birth to old age but are commoner in persons in the second decade of life. They are found with equal frequency in the male and the female, on the right and left sides, and involve the anterior surface of the epiglottis six times as frequently as they involve the posterior surface.[42] These growths are usually small but may reach large proportions, as in the case reported

33. Kallay, F.: Retentionszysten des Kehlkopfes, Monatsschr. Ohrenh. **76**:251-255 (June) 1942.

34. Jurasz, cited by Jacobi, M., and Rascoff, H.: Cyst of the Larynx in Infancy, Am. J. Dis. Child. **49**:448-459 (Feb.) 1935.

35. Park, J. H., Jr., and Israel, S.: Epiglottic Cysts in Infancy, South. M. J. **18**:128-131 (Feb.) 1925.

36. Chiari, cited by Park and Israel.[35]

37. Kahler, O.: Ein Beitrag zur Genese der Epiglottiscysten, Arch. Laryng. u. Rhin. **17**:8-13, 1905.

38. Louys, E.: Des kystes intralarynges et en particulier des kystes larynges branchiogènes, Thesis Geneva, Paris, Felix Alcan, 1900.

39. New, G. B., and Erich, J. B.: Congenital Cysts of the Larynx: Report of a Case, Arch. Otolaryng. **30**:943-949 (Dec.) 1939.

40. Woodruff, G. H.: Cyst of the Epiglottis and Other Laryngeal Cysts, Illinois M. J. **66**:569-573 (Dec.) 1934.

41. Jackson, C., and Jackson, C. L.: The Larynx and Its Diseases, Philadelphia, W. B. Saunders Company, 1937, p. 346.

42. Taylor, H. M.: Cyst of the Epiglottis, New York Med. J. & Med. Rec. **117**:357-358 (March 21) 1923.

by New.[43] They are usually single, sessile, and unilocular but may be multiple or pedunculated. The surface is glistening and often covered by vascular arborizations. The contents may be grayish, whitish, reddish, or yellowish. The wall is ordinarily thin and compressible but may be thick and firm to palpation. Hemorrhagic cysts are distinguished by their deep red or bluish color.

The two commonest symptoms of epiglottic cysts are foreign body sensation and dysphagia. If the laryngeal introitus is encroached upon by the body of the growth or by a distorted and displaced epiglottis, then dyspnea, cough, or hoarseness may be present. The dyspnea at times occurs in the form of acute distressing attacks, especially when the patient assumes the prone position. Taylor [42] described a case in which nocturnal choking spells due to a cyst of the epiglottis persisted after the cyst was removed owing to an atrophic epiglottis that prolapsed into the laryngeal introitus. The symptom cleared after the upper half of the epiglottis was amputated.

The diagnosis of epiglottic cysts in the adult can usually be made by mirror or direct laryngoscopy or in some instances by direct visualization and/or palpation through the oral cavity after forcible depression of the tongue.

The treatment of epiglottic cysts is conditioned somewhat by such factors as size and location of the growth, degree of dyspnea, age, and general physical status of the patient. Rarely, these cysts undergo spontaneous rupture or traumatic rupture from digital manipulation by the patient. The retention or mucous cysts have been treated at times by puncture or by removal of a section of the wall with punch forceps or cautery. The base, or wall, of the cyst if incompletely removed, may or may not be cauterized with the actual current. Postoperative hemorrhage is usually not a troublesome factor, although the two cases reported by Freudenthal are an exception to this rule. Patients who are severely dyspneic may require a preliminary tracheotomy, and infected cysts are best incised prior to any attempt at removal. The operative approach to cysts of the epiglottis may be made through the mouth by forcible depression of the tongue, or by means of direct or suspension laryngoscopy, employing snare, forceps, or dissection as indicated. In most instances these growths can be removed by direct laryngoscopy. If the epiglottic cysts involve other portions of the larynx, a thyrotomy with or without preceding tracheotomy may be necessary.

Case 6.—S. G. P., a white woman, aged 52 years, referred by Dr. Vernon Offutt, was first seen in the office Sept. 3, 1948, with the chief complaint of a sense of fulness in the throat and slight hoarseness following a respiratory tract infection one month before. The patient stated that one year previously she had some "tumors" in her throat drained by another physician, and thereafter she was asymptomatic until the onset of the respiratory infection mentioned above.

Examination of the ears, nose, and throat disclosed essentially normal conditions except for the presence of three smooth yellowish cystic-appearing masses on the anterior surface of the epiglottis noted on mirror laryngoscopy. One of these was a large sessile growth, situated to the left of the midline, which completely filled the left vallecula. Numerous vascular arborizations covered its surface. The two remaining tumors were smaller, pedunculated, and situated to the right of the midline, and no vascular arborizations were present. No masses were palpated in the neck.

The patient was hospitalized Sept. 7, for removal of the cysts. The results of the general physical examination were essentially normal, and the findings on routine laboratory studies were within normal limits. The operation was done on the day of admission with the area under

43. New, G. B.: Cysts of the Larynx, Journal Lancet **37**:99-102 (Feb.) 1917.

local anesthesia. The larynx was exposed with a Jackson adolescent type laryngoscope and the base of the tongue displaced with the tip of the instrument. The cysts were amputated flush with the anterior surface of the epiglottis by means of a ring-shaped laryngeal cutting forceps. One cyst was removed without rupture, and the contents of the remaining cysts were a thick yellowish material. Hemorrhage was negligible; the postoperative course was uneventful, and the patient was discharged from the hospital the following day.

Pathologist's Report.—Gross Description (fig. 3): The tissue consisted of four large sheets of material, the largest measuring 2.5 cm. in length, 1 cm. in diameter, and 1 mm. in thickness. The two smaller masses measured 1.5 cm. by 1 by 0.2 cm. The masses appeared to be cystic.

Microscopic Description: The sections showed a thin cyst wall composed predominantly of lymphoid tissue. The surface was covered with stratified squamous epithelium, and the greater portion of the cyst lining was squamous epithelium also. The final diagnosis was simple epithelial cysts.

Follow-Up Observations.—The patient was last seen Aug. 18, 1950, at which time there was no recurrence of the cysts.

CASE 7.—S. R. C., a white man, aged 56 years, referred by Dr. Vernon Offutt, was seen in the office for the first time Sept. 10, 1948, with a single complaint of chronic cough of many years' duration.

Examination of the ears, nose, and throat disclosed essentially normal conditions except for a generalized congestion of the respiratory mucosa and the presence of a large smooth sessile cystic mass situated on the anterior surface of the epiglottis to the left of the midline. Numerous vascular arborizations were present on the surface of the growth. Reexamination was

Fig. 3 (case 6).—Multiple epithelium-cysts of the epiglottis. The small cyst in the center was removed without rupture.

made one month later after the patient had stopped heavy cigarette smoking. At this time, he no longer coughed, and the appearance of the cyst was the same as on the previous examination.

The patient was hospitalized Oct. 6 for removal of the cyst under local anesthesia. The general physical examination disclosed essentially normal conditions, and the results of routine laboratory studies were within normal limits. The operative technique was identical with that employed in case 6. The cyst contents were thick and yellowish. Hemorrhage was moderately free for a few seconds but subsided under pressure. The postoperative course was uneventful, and the patient was discharged the following day.

Pathologist's Report.—Gross Description: The tissue submitted consisted of two fragments, the larger piece measuring 2 by 1.5 cm. and 0.4 mm. thick and the smaller 1 cm. long, 5 mm. in diameter, and 2 mm. thick. The surface was yellowish gray, and it was soft to touch. The tissue appeared to be from a very thin-walled cystic space.

Microscopic Description: The tissue submitted was from a simple cyst, the walls of which appeared to be lined with cells compatible with mesothelial cells. The lining membrane was indistinct in certain localities. The cyst wall was composed predominantly of lymphoid tissue and covered on the outside by stratified squamous epithelium. In all sections the cells were well differentiated. The final diagnosis was simple cyst of the epiglottis compatible with lymphangiectatic cyst.

Follow-Up Observations.—The patient was last seen Dec. 4, 1950, at which time there was no evidence of recurrence of the cyst.

CASE 8.—C. H., a white boy, aged 10 years, was first seen in the office Jan. 24, 1949, with the chief complaint of headache, postnasal drainage, and nasal obstruction. There were no symptoms referable to the larynx.

Examination of the ears, nose, and throat revealed a congestion of the nasal passages and a diffuse lymphoid hyperplasia of the nasopharynx. Mirror laryngoscopy showed the presence of a smooth pinkish sessile growth on the anterior surface of the epiglottis to the left of the midline. Vascular arborizations were present, and the mass completely filled the left vallecula. Roentgenograms were reported as indicating clear nasal sinuses.

The patient was hospitalized Feb. 4, for removal of the cyst under local anesthesia. The general physical examination (by Dr. W. E. Keiter) revealed essentially normal conditions, and the results of routine laboratory studies were within normal limits. The operative technique was identical with that employed in the previous cases. The cyst contents were a thin yellowish material. Hemorrhage was slight; the postoperative course was uneventful, and the patient was discharged the following day.

The pathologist reported that the cystic mass was made up of a space lined by compressed cells and containing stringy material. The final diagnosis was mucous cyst.

The patient was last seen Aug. 5, 1950, at which time there was no evidence of recurrence of the cyst.

Comment.—Three additional cases of epiglottic cysts without symptoms were discovered on routine mirror laryngoscopy. In one of these the cyst ruptured spontaneously and re-formed during the period that the patient was under observation. The presence of small masses of lymphoid tissue often noted on the anterior surface of the epiglottis brings into consideration the possibility of inflammation of this tissue as an etiological agent in the formation of retention cysts of the epiglottis. In only one of the six cases observed were there symptoms which could be attributed to the epiglottic cysts.

Lateral Cervical Cyst Associated with Edema of the Larynx

Many case reports of lateral cervical cysts recorded in the literature between 1903 and 1948 were reviewed, but no exact counterpart of the case to be presented was found.

Case 9.—C. D. B., a white man, aged 62 years, referred by Drs. H. B. Ivey and Harold Wolfe, was first seen in the office, Jan. 6, 1947, with the chief complaint of a painless swelling in the right side of the neck, hoarseness, chronic sore throat, and occasional difficulty in swallowing of about three months' duration. About nine months previously, the neck swelling was first noted while the patient was shaving. It lasted two or three days, disappeared, and recurred in November 1946 to enlarge gradually thereafter. At the time of the recurrence a mild hoarseness developed; this was intermittent at first but later became constant. One month later a persistent mild sore throat and occasional difficulty in swallowing developed. The general health was good except for attacks of "rheumatism" and elevation of the blood pressure.

Examination of the ears, nose, and throat disclosed essentially normal conditions except for moderate clouding of the antrums on transillumination. Mirror laryngoscopy revealed a moderate edema of the right side of the larynx with limitation of motion of the right vocal cord. Palpation of the neck disclosed the presence of a small, smooth, slightly firm, movable mass on the right side at the level of the middle third of the sternocleidomastoid muscle. The mass was not tender to palpation and transmitted light poorly, and the overlying skin was not adherent. The esophagus and chest appeared on roentgenograms to be within normal limits.

The patient was hospitalized Jan. 13, 1947, for further studies. The general physical examination disclosed conditions essentially normal except for a blood pressure of 180/100. The results of routine laboratory studies were within normal limits. Soft tissue roentgenograms of the neck revealed that the mass did not have any extensive prolongations, and roentgenograms of the cervical spine showed changes that were consistent with a diagnosis of osteoarthritis. Dr. J. L. Etherington performed direct laryngoscopy in my absence, but no additional information concerning the larynx was obtained. At the same time, he aspirated 5 cc. of thick foul yellowish material from the cervical mass. This material was subsequently found to be sterile on culture, and no tubercle bacilli were identified on direct smear and culture. No study was

made for cholesterol crystals. The patient was discharged from the hospital with a diagnosis of lateral cervical cyst.

The patient was readmitted to the hospital, and the cyst was removed by blunt dissection under local anesthesia Jan. 25. The growth was a smooth grayish yellow mass that extended down to, but was not adherent to, the carotid sheath. Several lymph nodes were attached to the outer wall of the cyst, and no fistula was found. The postoperative course was uneventful, the patient being discharged from the hospital Feb. 1, 1947.

Pathologist's Report.—Gross Description: The tissue submitted consisted of an irregular mass and two small fragments which resembled lymph nodes. The large mass was soft to palpation, ovoid in shape, and measured 4 by 2.5 by 2.5 cm. It grossly resembled a cystlike structure. The mass was dark gray with some areas of discoloration, and its surface was smooth in some parts and rough in others. The wall of the cyst measured less than 1 mm., and the internal surface was finely roughened. The contents were a friable grayish yellow cheeselike material which shelled out easily.

Microscopic Description: Sections through the cystlike structure showed it to be lined with a thin layer of stratified squamous epithelium. The greater part of the wall of this structure, however, was made up of lymphoid tissue showing characteristic lymphoid nodules here and there. Sections through the lymph nodes showed the usual architecture to be fairly well preserved. The final diagnosis was branchial cyst and chronic lymphadenitis.

Postoperative Course.—The edema of the larynx subsided, the motility of the right vocal cord returned to normal, and the dysphagia disappeared within a few weeks after removal of the cyst. The patient was last seen in the office Jan. 3, 1948, and last contacted by letter May 14, 1949, at which times there was no recurrence of the cyst.

Comment.—It is difficult to explain the laryngeal edema and dysphagia in this case. It is possible that such findings might be explained on the basis of a direct connection of the cyst with the larynx or on the basis of the mechanical pressure exerted by the cyst on the surrounding soft tissues. Only two cases of lateral cervical cysts with laryngeal connections were encountered in the literature. Herman [44] reported a unique case of a double lateral cervical cyst complicated by carcinoma of the larynx, and one of the double cysts had a fistulous connection with the larynx. Thompson [45] reported the case of a patient with dysphagia, pain, aphonia, and fixation of the left vocal cord. At operation, a lateral cervical cyst was found attached to the left lamella of the larynx and the greater cornu of the hyoid bone, and the symptoms disappeared after removal of the cyst. There was no gross connection between the cyst and the larynx in the case under consideration. Mechanical obstruction by the cyst to the venous and/or lymphatic return from the larynx seems to be the most logical explanation for the laryngeal edema. The dysphagia probably resulted from pressure on the pharyngoesophageal area by the bulk of the cyst. It does not seem likely that the dysphagia was due to compression of the vagus nerve, since there was no paralysis of the right vocal cord.

Infected Ear Pits (Congenital Auricular Fistulas)

Ear pits do not occur frequently. Urbantschitsch [46] reported an incidence of 0.19 per cent in a group of 2,000 patients, and Stannus [47] found ear pitting in 5.2

44. Herman, A. L.: Double Branchial Cysts Complicated by Carcinoma of the Larynx, Minnesota Med. **14**:555-557 (June) 1931.

45. Thompson, J. W.: A Case of Branchial Cyst, Lancet **1**:76 (Jan. 8) 1927.

46. Urbantschitsch, V.: Concerning the So-Called Fistula Auris Congenita: Anomaly of Formation, Edinburgh M. J. **23**:690-695 (Feb.) 1878.

47. Stannus, H. S.: Congenital Anomalies in a Native African Race, Biometrika **10**:1-24 (April) 1914.

per cent of females and 3.6 per cent of males in a group of 6,491 African Negroes. In this country, Selkirk [48] examined school children for evidence of ear pitting and found an incidence of 0.9 per cent in 3,660 whites and an incidence of 5.2 per cent in 346 Negroes. The condition occurs more frequently in Orientals, especially the Chinese.

Heusinger [49] directed attention to the congenital nature of ear pits, and Connon [50] concluded that they are inherited as an incomplete dominant of variable occurrence without sex difference. His conclusions are in essential agreement with those of Kindred,[51] Quelprud,[52] Edmonds and Keeler,[53] and McDonough.[54] Pipkin and Pipkin [55] reported a pedigree in which dominant albinism and ear pits were inherited in a Negro family in such a way as to suggest a possible linkage of the two genes. The intertubercular theory of His, the branchial cleft hypothesis of Virchow, and the facial cleft theory are the three main concepts which have been advanced to explain the presence of ear pits, the His theory being generally accepted. There are valid arguments against the acceptance of each theory.

Druss and Allen,[56] Becker and Brunschwig,[57] and others studied certain aspects of the histopathological features of ear pits, and Congdon,[58] Caldera,[59] Dragisic,[60] Schuller,[61] Zöllner,[62] and Fournier [63] made substantial contributions to the clinical anatomy and clinical features of this anomaly. Ear pits may be associated with pigmentation of the adjacent skin, as observed by Selkirk,[48] with a pigmented mole,

48. Selkirk, T. K.: Congenital Aural Fistula, Am. J. Dis. Child. **49**:431-447 (Feb.) 1935.

49. von Heusinger, K. F.: Hals-Kiemen-Fisteln von noch nicht beobachteter Form, Arch. path. Anat. **29**:358-380, 1864.

50. Connon, F. E.: The Inheritance of Ear Pits in 6 Generations of a Family, J. Hered. **32**:413-414 (Nov.) 1941.

51. Kindred, J. E.: Inheritance of a Pit in the Skin of the Left Ear, J. Hered. **12**:366-367 (Oct.) 1921.

52. Quelprud, T.: Ear Pit and Its Inheritance, J. Hered. **31**:379-384 (Sept.) 1940.

53. Edmonds, H. W., and Keeler, C. E.: Natural "Earring" Holes: Inherited Sinuses of Ear Lobe, J. Hered. **31**:507-510 (Dec.) 1940.

54. McDonough, E. S.: On Inheritance of Ear Pit, J. Hered. **32**:169-170 (May) 1941.

55. Pipkin, A. C., and Pipkin, S. B.: Ear Pits and Albinism in a Negro Family, J. Hered. **34**:240-242 (Aug.) 1943.

56. Druss, J. G., and Allen, B.: Congenital Fistula of the Neck Communicating with the Middle Ear, Arch. Otolaryng. **31**:437-443 (March) 1940.

57. Becker, S. W., and Brunschwig, A.: Sinus Preauricularis (Fistula Preauricularis Congenita), Am. J. Surg. **24**:174-177 (April) 1934.

58. Congdon, E. D.; Rowhanavongse, S., and Varamisara, P.: Human Congenital Auricular and Juxta-Auricular Fossae, Sinuses, and Scars (Including the So-Called Aural and Auricular Fistulae) and the Bearing of Their Anatomy upon the Theories of Their Genesis, Am. J. Anat. **51**:439-463 (Nov.) 1932.

59. Caldera, C.: Nuova varietà difistula auris congenita e contemporaneo addoppiamento del condotto uditivo esterno, Arch. ital. otol. **33**:55-59, 1922.

60. Dragišić, B.: Angeborene Ohrfisteln und ihre differential-diagnostische Bedeutung im Kindesalter, Wien. med. Wchnschr. **86**:748-750 (July 4) 1936.

61. Schuller, J.: Zur Vererbung der Fistula auris bzw. auriculae congenita: zugleich ein klinischer Beitrag, München. med. Wchnschr. **76**:160-162 (Jan. 25) 1929.

62. Zöllner, F.: Fehldiagnosen, verursacht durch angeborene Fisteln und Cysten an Ohr und Hals, Ztschr. Hals-, Nasen- u. Ohrenh. **32**:54-61, 1932.

63. Fournier, G.: À propos d'un cas de fistule congénitale de l'oreille, Rev. laryng. **40**:145-156 (April 15) 1919.

as stressed by Aird,[64] or with congenital patchy scarring of the skin of the cheek. Ear pits are occasionally associated with other deformities of the outer ear or other developmental anomalies. Baumgartner and Steindel,[65] Urbantschitsch,[66] Hynman and Light,[66] Bull,[67] and Evans [68] reported cases of congenital auricular fistulas which were associated with either unilateral or bilateral cervical fistulas. Gelston and Sappington [69] and Selkirk [48] each reported a case of ear pit seen in conjunction with congenital paralysis of the seventh nerve and deformity of the external ear. Dragisic [60] and Keith [70] in their study found ear pits associated with other developmental anomalies.

Infection is most likely to develop in the preauricular type of congenital aural fistulas. There may be a discharge of malodorous pus which is often preceded by redness, itching, and discomfort about the orifice of the sinus; recurrent abscess formation with spontaneous rupture, or surgical incision, with or without healing; facial edema from cellulitis; recurrent or chronic ulceration of the skin of the face or ear, which often simulates a tuberculous process and, occasionally, the development of secondary fistulas. Retention cysts which may or may not become infected are formed if the lumen of the sinus becomes obstructed. The anterior auricular lymph nodes may become inflamed secondary to an infection of congenital aural fistulas and give rise to acute or chronic lesions of the face, as reported by Hamann.[71] Rischbieth [72] observed a female patient with an ear pit that discharged only during menses.

The diagnosis of uncomplicated ear pits can usually be made by inspection, but a familial tendency is vital to the diagnosis of some types. Sounding and injection of a contrast medium followed by roentgenograms give valuable preoperative information.

The keynote to the treatment of infected ear pits is complete excision of the fistulous tract when this can be accomplished. If tissue destruction from chronic inflammation is present, excision may be combined with electrocoagulation of the diseased tissues. Permanent spontaneous healing of infected fistulas is rare. Since infection rarely supervenes in these fistulas, surgery is rarely indicated, as evidenced

64. Aird, I.: Ear Pit (Congenital Aural and Pre-Auricular Fistula), Edinburgh M. J. **53**:498-507 (Sept.) 1946.

65. Baumgartner, C. J., and Steindel, S.: Differential Diagnosis Between Thymic Duct Fistulas and Branchial Cleft Fistulas, Am. J. Surg. **59**:99-103 (Jan.) 1943.

66. Hynman, O. R., and Light, G.: The Branchial Apparatus, Arch. Surg. **19**:410-452 (Sept.) 1929.

67. Bull, O.: Fistulae Fissurarum Branchialium, Together with Peculiar Malformation of the Membranae Tympani, Arch. Otol. **17**:36-38, 1888.

68. Evans, J. H.: Case of Symmetrical Bilateral Branchial Fistulae with Symmetrical Bilateral Helical Fistulae and Misshapen Aural Pinnae, Rep. Soc. Study Dis. Child. **4**:114-116 (Jan. 19) 1903-1904.

69. Gelston, C. F., and Sappington, E. E.: Congenital Malformation of the Auricle Associated with Paralysis of the Facial Nerve, Arch. Pediat. **49**:730-742 (Nov.) 1932.

70. Keith, A.: Congenital Malformations of Palate, Face, and Neck, Brit. M. J. **2**:438-441 (Aug. 21) 1909.

71. Hamann, C. A.: Cases of Congenital Auricular and Cervical Fistulae, Cleveland M. Gaz. **9**:110-112 (Jan.) 1893-1894.

72. Rischbieth, H.: Congenital Auricular Fistula, M. J. Australia **2**:251 (Sept.) 1916.

by the report of Pastore and Erich [73] who found only 13 patients requiring operation at the Mayo Clinic over a period of 20 years. Miller and Moore [74] recently reported on nine patients surgically treated at the Cleveland Clinic.

CASE 10.—B. K., a Negro girl, aged 11 years, referred by Drs. Paul Meyers and Vernon Offutt, was seen in the office for the first time July 31, 1948. The patient's chief complaint was that of a "running sore" in front of the left ear of five years' duration. The mother of the patient stated that six years previously a "rising" (abscess) developed on the patient's left ear, and at this time a previously unrecognized opening on the ear was noted. The infection subsided quickly and was followed one month later by a similar "rising" in front of the left ear, which was incised by the family physician. One year later, there was a recurrence of the abscess in the latter area with spontaneous rupture. Since that time there had been a chronic sore in this region which was constantly crusted and which would periodically drain small amounts of foul pus. The opening on the ear also drained intermittently. Various forms of treatment were tried without success.

Examination of the ears, nose, and throat disclosed conditions essentially normal except for the presence of hypertrophied tonsils and adenoids and the aural lesion. Along the anterior

Fig. 4 (case 10).—Congenital aural fistula of the anterior marginal helicine type with chronic ulceration of the preauricular region. The history suggests that the ulceration due to the infected fistula occurred in an area of congenital preauricular scarring. The helicine orifice of the fistula is scarcely visible.

margin of the ascending limb of the helix of the left ear there was a small opening from which exuded foul pus. A probe was introduced into the opening for a distance of several millimeters. In the left preauricular region there was a crusted area measuring about 10 mm. in diameter, and after removal of the crust a superficial ulceration of the skin with a small opening in the center was noted. The skin surrounding the ulcer had a very finely wrinkled appearance (fig. 4.). Chloriodized oil (iodochlorol®) was injected into the helicine opening and was seen to escape through the ulcerated area. Roentgenograms made immediately afterward showed that the sinus tract was superficial.

The patient was hospitalized Aug. 18. The general physical examination (by Drs. W. E. Keiter and Dan Boyette) was reported to have disclosed essentially normal conditions, and the results of routine laboratory studies were within normal limits. The fistulous tract was excised by sharp dissection with the patient under ether anesthesia on the day of admission. In the

73. Pastore, P. N., and Erich, J. B.: Congenital Preauricular Cysts and Fistulas, Arch. Otolaryng. **36**:120-125 (July) 1942.

74. Miller, J. B., and Moore, P. M., Jr.: Fistula Auris Congenita, Arch. Otolaryng. **51**:245-257 (Feb.) 1950.

first part of its course, the sinus ran downward along the anterior margin of the ascending limb of the helix, passing deep to the spina helicis. It then turned forward to terminate in the ulcerated preauricular lesion. The skin surrounding the ulcer was found to be very friable and bled easily. Because of the superficial nature of this inflammation, coagulation of the tissues was not done. The postoperative course was uneventful, and the patient was discharged from the hospital Aug. 20, 1948.

Pathologist's Report.—Gross Description: The tissue submitted was a stringy mass measuring 2 cm. in length, 3 mm. in diameter, and 2 mm. in thickness. The material cut with a slightly gritty sensation.

Microscopic Description: Sections through this material showed a thickened squamous epithelium-lined cystic space. All the cells were clear and distinct in outline and well differentiated. There was a small fragment of cartilage present in the tissue, which appeared to have been removed at the time of surgery. Otherwise, one could see squamous epithelium on the surface. The epithelium showed some increased pigmentation of the malpighian layer. The final diagnosis was a chronically inflamed squamous epithelium-lined sinus tract.

Follow-Up Observations.—The patient was last seen May 6, 1949, at which it was found that there was no recurrence of the previous condition.

Comment.—Two additional cases of infected congenital auricular fistulas were observed during this period. In both of these the infection promptly subsided with antibiotic therapy, and there has been no recurrence to date. Prompt healing followed surgical extirpation of the infected sinus tract in the case presented. The wrinkled appearance of the skin surrounding the preauricular ulceration suggests the presence of a congenital scarring in this area, but the history of its presence prior to the onset of infection is not too reliable. The improved cosmetic appearance following surgery was definitely reflected in the patient's personality.

III. GRANULOMAS

Granulomas of the parotid region are not common, and no counterpart of the case to be reported was found in the literature from 1925 through 1948.

CASE 11.—J. H., a Negro man, aged 34 years, was first seen in the office Feb. 23, 1948. He complained of a painful swelling in the right parotid region and difficulty in opening his mouth. About 10 years previously he had first noted a "knot" in front of his right ear, and five years later this began slowly to increase in size. In December 1946 mild pain developed in the growth, and the patient consulted an otolaryngologist, who performed a biopsy. The pathologist reported chronic inflammation. The patient did not seek further medical attention until he was seen in the office. One week prior to this time, the mass became extremely painful without obvious increase in size and the patient had difficulty in opening his mouth.

Examination of the ears, nose, and throat revealed hypertrophied tonsils and clouding of the antrums on transillumination. Saliva of normal color was seen to flow from the right parotid duct, which could be probed for some distance without difficulty. Anterior to the right auricle was a large firm sessile slightly painful mass with the overlying skin adherent along the line of a linear scar. A small movable painless lymph node was palpated in the right postauricular region, and there was a moderate degree of trismus present. A tentative diagnosis of mixed tumor of the right parotid gland was made.

The patient was hospitalized Feb. 16, 1948. The general physical examination disclosed essentially normal conditions, and the findings of routine laboratory studies were within normal limits. The tumor was removed by sharp dissection under 1 per cent procaine hydrochloride anesthesia preceded by heavy preoperative sedation. It had a dark grayish appearance and was adherent at one point to the lateral surface of the parotid gland and to the tragus and helix of the auricle. A portion of the tumor projected into the retromandibular space. A small part of the lateral surface of the parotid gland was resected in order to remove the growth completely. On the first postoperative day there was a profuse flow of saliva from the wound, and a facial

paralysis of the peripheral type was present. The patient was discharged from the hospital 10 days later.

Pathologist's Report.—Gross Description (fig. 5): The tissue submitted was a large mass compatible with a tumor from the right parotid region. It measured 5 cm. in length, 3 cm. in diameter, and 2.5 cm. in thickness. It was a mottled yellowish brown and bluish purple throughout. On section the surface was shown to be a light yellowish brown, and running through this colored material were numerous gray trabeculae. The material cut easily and appeared to be lobulated.

Microscopic Description: This tumor mass microscopically showed a predominantly chronic granulomatous reaction. One section of the tumor showed glands resembling acini of the parotid. Scattered through the entire section were numerous vacuolated spaces suggesting that fat had dissolved out in the fixing process. Numerous separate lobulated or partially encapsulated spaces were seen which contained red blood cells, hyaline material, lymphocytes, and degenerated cells. Other sections showed the same lobular type of structure in which there was only a diffuse lymphocytic infiltration with the presence of giant cells. Not all areas showed these giant cells, however. Coursing through these previously described lobulated spaces

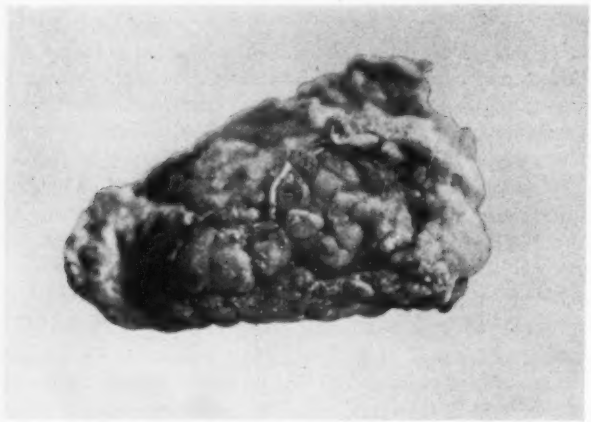

Fig. 5 (case 11).—Chronic granuloma of possible fungous origin removed from the right parotid region.

was a considerable amount of fibrous tissue stroma. The cells in the stroma were clear and distinct in outline and well differentiated. Lymphocytic infiltration was noted around numerous blood vessels, some of which were dilated and filled with red blood cells. Sections previously made from the biopsy material were reviewed, and the original diagnosis of chronic inflammation was confirmed. The final diagnosis was chronic granulomatous inflammation. The type of reaction here suggested some type of fungus infection.

Postoperative Course.—The salivary fistula healed in about three weeks, and the facial nerve recovered its function in about three months. The patient was last seen Dec. 2, 1950, at which time there was no evidence of recurrence of the growth.

Comment.—This unusual case presented some of the features of a mixed tumor of the parotid gland. The complication of the salivary fistula was anticipated. The facial paralysis was not expected, and it apparently resulted from injury to this nerve in dissecting the retromandibular portion of the growth. There was no history or evidence of foreign body, and the cause for this granuloma was never determined.

Tuberculous Cervical Adenopathy Probably Influenced by Streptomycin Therapy

Children with enlarged cervical lymph nodes are seen commonly in the practice of otolaryngology, but cervical adenopathies of a tuberculous nature are, fortunately, relatively rare today. The decreased incidence of tuberculous cervical adenitis has been attributed in part to a safer milk supply, better isolation and care of tuberculous patients, the wide practice and improved methods of removing diseased tonsils and adenoids, and the advance in the general hygiene of the patients in all classes of the community.

Case 12.—L. D. S., a white boy, aged 5 years, referred by Drs. Lynwood Williams and Paul Meyers, was first seen in the office March 15, 1948, with a painless swelling in the right side of the neck. The mother of the patient stated that the mass developed about two years before, and the patient was thought to have mumps. Swelling of the neck on the left side present at this time subsided and never recurred. The persistent cervical swelling continued to enlarge gradually, especially after head colds. Within the following year, two abscesses developed in the middle third of the neck. One of these was incised by the family physician, and the other was treated by x-ray therapy, with spontaneous rupture. The sinuses resulting from each abscess drained for many months but eventually healed. The patient consumed large quantities of unpasteurized milk; his general health was excellent, and there were no other complaints. Numerous clinical and x-ray examinations of the chest failed to reveal any pathologic changes. A skin test for tuberculosis elicited a strongly positive reaction. The father of the patient had proved pulmonary tuberculosis.

Examination of the ears, nose, and throat disclosed the presence of hypertrophied tonsils and adenoids. The teeth were in good condition. Examination of the neck revealed the presence of a large smooth firm nontender mass at the angle of the jaw on the right side. There was limited movement of the mass, and the overlying skin was normal in appearance without adherence to the underlying tumor. Below the angle growth in the midcervical region were two small scars, beneath which were palpated several small shotty lymph nodes. A few small lymph nodes were also discovered in the left anterior cervical chain. There was no evidence of a fistula in the neck or right tonsillar region.

Removal of the tonsils and adenoids was advised but not accomplished until one month later because of poor cooperation on the part of the patient. At this time the results of the general physical examination and of the routine laboratory studies were found to be within normal limits. On the fourth postoperative day, the patient returned with a small acute abscess in the region of the old cervical scars. This was evacuated in the office and about 2 cc. of pus obtained. A culture from this material was later reported as disclosing short thick bacilli, and a direct smear and culture were subsequently reported to be negative for tubercle bacilli. Pathological studies of the tonsils and adenoids showed chronic inflammatory changes.

The patient did not return until a month later, at which time he had an acute cold with a draining sinus at the site of the previous abscess. One week later there was the first evidence of suppuration in the angle mass, which was not tender to palpation. There were no systemic symptoms and only a slight elevation of temperature. Hospitalization was refused, and the abscess was evacuated uneventfully in the office with ethyl chloride anesthesia, about 60 cc. of odorless pus being obtained. Cheeselike material in the abscess cavity was carefully removed with swabs and forceps. Studies for cholesterol crystals, tubercle bacilli, and fungi gave negative results. Microscopic sections made from the cheesy material showed completely necrotic tissue.

The patient again failed to return for a year, at which time he had a painless swelling in the right submandibular region and a draining sinus in the right midcervical area (fig. 6). Both of these conditions developed suddenly one week before and were not associated with systemic symptoms. The mother stated that there were no cervical swellings or sinuses for several months prior to the onset of the above episode. Examination at this time did not afford additional information, except for the presence of several carious lower molar teeth on each side. Hospitalization was again refused.

The patient returned one month later with suppuration in the submandibular mass, and this time consent for hospitalization was obtained. On admission, the temperature was 100.4 F., and it decreased daily until a normal level was reached. The results of general physical examination were again normal, and a dental consultant did not think that extractions were indicated at the time. Soft tissue roentgenograms revealed numerous areas of calcification in the right cervical region. The results of laboratory studies were essentially normal, except for the presence of a moderate leukocytosis. The patient was given 0.5 Gm. of dihydrostreptomycin sulfate twice daily during his hospital stay and for one month subsequent to his discharge from the hospital.

On April 2, 1949, the abscess was evacuated with the patient under ether anesthesia. Considerable granular pus was obtained, and a partly necrotic lymph node was removed. The postoperative course was uneventful, and the patient was discharged from the hospital one week later.

Tubercle bacilli were not identified in the pus obtained at operation by smear, culture, or guinea pig inoculation, and a culture for fungi was also negative. Sections made from the lymph node showed chronic granulomatous changes, and stains made from the same node failed to show any acid-fast organisms.

Fig. 6 (case 12).—Tuberculous adenitis of the submandibular lymph nodes which developed one year after involvement of the tonsillar lymph node.

Follow-Up Observations.—The patient was last seen in the office Sept. 24, 1949, at which time all cervical lesions were well healed, and reliable reports to date indicate that there has been no further recurrence of cervical swellings or draining sinuses.

Comment.—The diagnosis of tuberculous cervical adenitis was based on the history of drinking unpasteurized milk, positive tuberculin reaction, clinical features and clinical course of the disease, the x-ray evidence of calcified cervical lymph nodes, and history of pulmonary tuberculosis in one parent. It is believed that streptomycin therapy probably exerted a beneficial effect on this patient.

IV. ABERRANT SALIVARY GLAND TISSUE IN THE TONSILLAR FOSSA

The first case of aberrant salivary gland tissue in the tonsillar fossa was reported by Neumann in 1928.[75] O'Neil,[76] in 1948, reviewed the literature on this subject and

75. Neumann, H.: Schleimdrüse vom Tonsillenbette ausgehend, Wien. med. Wchnschr. **78**:650 (May 12) 1928.

76. O'Neil, J. J.: Aberrant Salivary Gland Tissue in Tonsillar Fossae, Eye, Ear, Nose & Throat Month. **27**:234-237 (May) 1948.

found that there were a total of six cases reported, to which he added a case of his own. This total did not include four cases mentioned by Davis and Donnelly in the discussion of a paper on this subject by Hitschler and Cope.[77]

CASE 13.—P. K., a white girl, aged 3 years, referred by Dr. O. W. Cranz, was seen in the office for the first time March 28, 1949. The mother of the patient stated that she had inspected the child's throat several times weekly after a severe attack of acute tonsillitis one month previously. Three days before, she had noted that the left tonsil seemed "pushed-out," and it was because of this unusual appearance that she sought medical advice.

Examination of the ears, nose, and throat revealed the presence of hypertrophic tonsils and adenoids and slight enlargement of the anterior cervical lymph nodes bilaterally. The tonsils were approximately equal in size, but the left tonsil was displaced in an anteromedial direction past the midline. Palpation of the left tonsil and surrounding area failed to reveal any findings of note.

The patient was hospitalized April 5, 1949. The general physical examination (by Drs. W. E. Keiter and Dan Boyette) disclosed essentially normal conditions, and the results of routine laboratory studies were within normal limits. The operation was performed on the day of the patient's admission. After removal of the tonsils and adenoids the left tonsillar fossa was inspected, and a small fragment of yellowish material was seen in the lower third. The mass was dissected free from its attachment to the posterior surface of the lower third of the anterior tonsillar pillar and adjacent tonsillar fossa. The gross specimen was soft to palpation and did

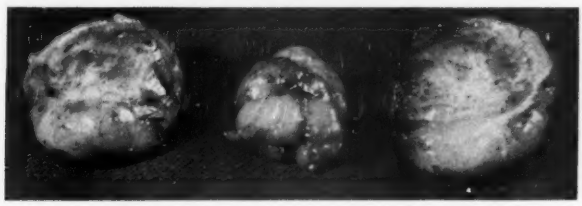

Fig. 7 (case 13).—Tonsils and aberrant salivary gland tissue (center).

not appear to be encapsulated. The postoperative course was uneventful, and the patient was discharged from the hospital the following day.

The tonsils, adenoids, and aberrant tissue were submitted for pathological study with a tentative diagnosis of fat or salivary gland tissue being made for the latter. Nothing of note was found on microscopic examination of the tonsils and adenoids.

Pathologist's Report.—Gross Description (fig. 7): The tissue submitted was an irregular mass measuring 1.4 cm., grayish over the outer surface with small nodulations present. On section the wall was found to be grayish and homogeneous in appearance.

Microscopic Description: Microscopic sections revealed a portion of a salivary gland. There were many glandular spaces lined by cells of both mucous and serous type. All the cells were well differentiated. The final diagnosis was salivary gland tissue.

Follow-Up Observations.—The patient was last seen Aug. 19, 1950, at which time there was no evidence of recurrence of the aberrant salivary gland tissue in the tonsillar fossa.

Comment.—A satisfactory preoperative diagnosis was not made. The appearance of the left tonsil suggested the presence of a growth lateral to the tonsil with displacement of this structure. A lymphoid tissue tumor was considered, but the findings did not seem to be wholly in accord with this diagnosis. This is believed to be the twelfth case of this nature to be reported.

77. Hitschler, W. J., and Cope, T. A.: Aberrant Salivary Gland in Tonsil Fossa, Arch. Otolaryng. **34**:174-176 (July) 1941.

SUMMARY

A number of relatively rare pathological conditions encountered in the office practice of otolaryngology are presented together with the essential features of their diagnosis and treatment, and appropriate comment on individual cases, or groups of cases, is made. The diagnosis and treatment in these cases represented a close cooperation between otolaryngologist, internist, radiologist, and pathologist. The value of routine examination of the larynx and regular periodic follow-up examinations is stressed.

Kinston Clinic.

IS HEARING LOSS DUE TO NUTRITIONAL DEFICIENCY?

Further Studies on the Influence of Vitamin A in Certain Types of Impaired Hearing

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IN A PRELIMINARY report,[1] a short time ago, I presented my experience with a new injectable vitamin A preparation in certain types of impaired hearing. Since the publication of this paper, Anderson, Zoller and Alexander [2] have conducted some interesting studies with the same preparation and concluded "that parenteral vitamin A therapy in massive doses is a valuable therapeutic agent in patients with deafness not amenable to the usual otolaryngologic methods of treatment."

These studies have aroused considerable interest, not only in the newer therapy suggested but in some of the older theories which were advanced in an effort to show a relation between nutritional deficiency and hardness of hearing.

This paper, therefore, has a twofold purpose, viz., (1) to clarify to some extent the possible role of vitamins in deafness and (2) to present results of more extended studies with anatola® [3] an improved injectable vitamin A product.

REVIEW OF LITERATURE

Before vitamins had been isolated, Mayer [4] believed there might be a relation between rickets and deafness of the otosclerotic type. In a child with well advanced rickets, he found that in the upper layers of the periosteal capsule there was bone-like tissue with deficiency of lime salts. After this study, cod liver oil was administered to persons with otosclerosis, with inconsistent results.[5] An interesting observation was the fact that in quite a few instances tinnitus was relieved, even though no improvement in hearing took place.

Early experimental work on animals suggested that changes in the labyrinthine capsule following a rickets-producing diet were similar to those of otosclerosis in humans [6] and "the analogies between the changes in experimental rickets and the

1. Lobel, M. J.: Clinical Studies with Parenteral Vitamin A Therapy in Deafness: Preliminary Report, Eye, Ear, Nose & Throat Monthly **28**:213 (May) 1949.

2. Anderson, J. R.; Zoller, H. J., and Alexander, L. W.: Observations on the Treatment of Deafness and Tinnitus with Parenteral Vitamin A in Massive Doses (Lobel), Eye, Ear, Nose & Throat Monthly **29**:75-79 (Feb.) 1950.

3. Manufactured by Parke, Davis & Company.

4. Mayer, O.: Untersuchungen über die Otosklerose, Leipzig, Alfred Holder, 1885.

5. Kauffman, A. B.: Deficiency Diseases of the Ear, Nose and Throat: 1. Otosclerosis; 2. Hyperplastic Ethmoiditis; A Preliminary Report, Laryngoscope **32**:50 (Jan.) 1922. Katz, L.: Sogennannte Otosclerose bei der Spongioserung des Schäfenbeins ohne Ankylose des Steigbügels mit partieller Degeneration des cortischen Organs und des Nervus cochlearus bei einer Taub gewordenen Katze, Arch. Ohrenh. **68**:122, 1906.

6. Aprile, V.: Sui rapporti tra rachitismo sperimentale e otosponsiosi, Valsalva **10**:649, 1945.

lesions which have been described in otosclerosis suggest that the latter condition may be a late result of rickets or a manifestation of a dietary deficiency state existent during adult life." [7] Manville [8] produced in rats deficient in vitamin A pyogenic infection of the upper respiratory tract which extended to the middle ear, and in some instances it became so severe that the vestibular apparatus also became involved, causing the animal to show circus movements.

Barlow,[9] on the other hand, performed a series of experiments on rats over a period of two years which did not confirm these findings. In his animals, "even in severe cases of rickets, the calcium content of the bony capsule is not appreciably altered. In rats on a diet deficient in vitamin D, there was no demonstrable loss of calcium and increase in canalization. The comparative study of . . . normal and rachitic rats showed no loss of calcium. This demonstrates that rickets is not an etiologic factor in deafness, and there is no reason to believe that a child that has once had rickets is likely to become deaf because of it." Nevertheless, Barlow,[10] in a later study, indicated that "Deficiency of vitamin A causing changes in the mucous membrane of the respiratory tract might be considered a possible factor in the production of changes in the soft tissue of the middle ear, which might become permanent."

In 1932 Cody [11] reported on extensive experimental studies dealing with the effects of avitaminosis on the ear, and impaired hearing was repeatedly demonstrated in rats deficient in vitamin A. Rosenfeld [12] administered cod liver oil with epinephrine and calcium to 18 persons with otosclerosis, on the premise that otosclerosis is a localized form of osteomalacia. Tinnitus was markedly reduced or disappeared altogether, and in many the hearing capacity was improved.

Gray,[13] in 1934, studying otosclerosis, pointed out that "the subjects of otosclerosis are, apart from their deafness, perfectly normal individuals with ordinary average health . . . . The deafness of otosclerosis is to a large extent functional, and is the result of the insufficient supply of blood to all the nerve structures concerned in the perception of sound." In spite of Gray's observation, many physicians continued to use vitamins in the management of deafness. Kahan [14] tried various combinations and found yeast, along with thermotherapy, most valuable. Char-

7. Kauffman, A. B.; Creekmur, F., and Schultz, O. T.: Changes in the Temporal Bones in Experimental Rickets: Their Relation to Otosclerosis, J. A. M. A. **80**:681 (March 10) 1923.

8. Manville, I. A.: Pathologic Changes Occurring in White Rats Raised on Diets Deficient in Vitamin A, Arch. Int. Med. **35**:549 (May) 1925.

9. Barlow, R. A.: Does Vitamin-Deficient Diet Cause Deafness? Results of Animal Experimentation, Laryngoscope **37**:640 (Sept.) 1927.

10. Barlow, R. A.: Otologic and Other Manifestations of Diet Deficient in Vitamins: Animal Experimentation, Arch. Otolaryng. **8**:629 (Dec.) 1928.

11. Cody, C. C.: Relation of Vitamins A, D, B, and G to Otolaryngology, Arch Otolaryng. **16**:661 (Nov.) 1932.

12. Rosenfeld, W.: Neue Richtlinien im Kampfe gegen die Otosklerose, Ohren-, Nasen-u. Kehlkopth. **134**:33 (Jan. 20) 1933.

13. Gray, A. A.: The Otosclerosis Problem: Including Reports of Two Cases Pathologically Examined, Proc. Roy. Soc. Med. **27**:1179 (July) 1934.

14. Kahan, D. S.: L'importance des vitamines dans la thérapeutique de l'otosclérose, Rev. laryng. **55**:1171 (Nov.) 1934.

schak [15] demonstrated improved hearing and disappearance of tinnitus in 12 of 15 patients with deafness treated with irradiated dried yeast. Then Selfridge [16] began an extended clinical study of the use of vitamins in deafness. He felt that degeneration of the nerve is the most important factor in otosclerosis and that "it is a nutritional disease depending on altered function of vasomotor nervous system, and that the bony changes at the footplate of the stapes and in other regions are due to a trophoneurosis." He found vitamin B_1 and nicotinic acid most beneficial in deafness. In over 30 cases he claimed audiometric improvements averaging 5 to 10 decibels throughout the tone range but in some cases 15 to 25 decibels for the lower tones.[17]

The addition of carotene did not produce any further change in hearing, although in a later report [18] he emphasized that lack of vitamins A, B and C brings about changes in the eighth nerve (auditory nerve) which would affect hearing.

Guggenheim [19] stressed the importance of proper nutrition in otosclerosis. Since "otosclerosis is both a bone disease and a neural disorder," even though an artificial fistula was successful it could not prevent further deterioration of the neural mechanism. With a regimen directed toward "reversal of halisteresis, regeneration of damaged neural mechanism by dietary regulation, and giving calcium phosphate and vitamins," in three years' time Guggenheim and Guggenheim [19b] claimed to have produced "improvement in hearing far greater than has any fistula operation thus far reported." The vitamins given were D, B complex, C and A. Babbitt [20] also reported "dramatic results" with a combination of vitamin B complex with liver and iron in deafness.

About this time Mellanby [21] made his report of production of deafness in young animals by a diet deficient in vitamin A. Previously [22] he had noted there was considerable degeneration of the vestibular division of the eighth nerve and the cochlear nerve in vitamin-deficient dogs. In the latter experiment, deafness was demonstrated by the animals' behavior. Mellanby explained the deafness was probably caused by a disorganization of the activity of osteoblasts and osteoclasts of the

15. Charschak, E.: Ein Versuch, die Otosklerose mit bestrahlten Hefen zu behandeln: Vorläufige Mitteilung, Acta oto-laryng. **23**:445, 1936.

16. Selfridge, G.: Can Certain Diseases of the Ear, Nose and Throat, Especially of the Eighth Nerve, Be Classified as "Deficiency Disease"? Laryngoscope **46**:85 (Feb.) 1936.

17. Selfridge, G.: Nicotinic Acid and the Eighth Nerve: A Preliminary Report, Ann. Otol., Rhin. & Laryng. **48**:39 (March) 1939; The Eighth Nerve in Relation to Thiamine Chloride and Nicotinic Acid: A Comparative Study, ibid. **48**:419 (June) 1939; Eighth Nerve High Tone Deafness from Nutritional Standpoint (Further Contribution), ibid. **48**:608 (Sept.) 1939.

18. Selfridge, G.: A Survey of the Relation Between Nutrition and the Ear, Ann. Otol., Rhin. & Laryng. **49**:674 (Sept.) 1940.

19. (*a*) Guggenheim, L. K.: On the Diagnosis and Treatment of Otosclerosis, Am. J. Surg. **42**:156 (Oct.) 1938. (*b*) Guggenheim, L. K., and Guggenheim, P.: Artificial Fistula in Cases of Otosclerosis, Arch. Otolaryng. **32**:1 (July) 1940. (*c*) Guggenheim, L. K.: Treatment of Deafness, Laryngoscope **50**:773 (Aug.) 1940.

20. Babbitt, J. A., in discussion on C. S. Nash: A Study in the Treatment of Deafness, Arch. Otolaryng. **28**:1029 (Dec.) 1938.

21. Mellanby, E.: Experimental Production of Deafness in Young Animals by Diet, J. Physiol. **94**:380 (Dec. 14) 1938.

22. Mellanby, E.: Nutrition and Disease: The Interaction of Clinical and Experimental Work, Edinburgh, Oliver & Boyd, 1934.

bone cells, resulting from lack of vitamin A, which causes bony overgrowth in the modiolus and periosteal layer of the labyrinth capsule. This bony overgrowth presses and stretches the nerve tissues, thus causing inhibition of transmission of the perception of sound. Later [23] it was demonstrated that if vitamin A was added to the diet during the animals' growth the osteoclastic and osteoblastic activity would regress.

Wolbach and Bessey [24] made a similar study and demonstrated deafness in animals deficient in vitamin A. However, they believed the pressure on the nerve was due to a continual growth of nerves after bone growth had ceased. On the other hand, Loch [25] reported that lack of vitamin A in rats resulted in new bone formation in the periosteal layer. Perlman and Willard [26] produced similar changes in rabbits on a vitamin A-deficient diet, but these writers concluded good cochlear function was retained in spite of compression and stretching of the nerve fibers.

In clinical studies with vitamin therapy in deafness, there have been variable results. Evans [27] prescribed yeast without obtaining marked improvement in tinnitus or hearing. Likewise Baer [28] was unable to alter the hearing with a combination of vitamins B_1 and C, although thiamine was effective in the treatment of tinnitus aurium, vertigo and other associated manifestations. However, Kubomura [29] treated a 22 year old patient suffering from deafness and tinnitus with vitamin B_1 administered parenterally and obtained good results. Childrey [30] suggested that vitamin B complex, especially thiamine hydrochloride, may be used as a preventive measure in deafness along with other routine measures. He does not believe, however, that it will be of much benefit unless there is definite deficiency of the vitamin.

In 1940, Jones [31] proposed an embryologic approach in the application of vitamins to disorders of the ear, nose and throat and studied extensively this phase of the subject. He mentioned that "tissues of the ectoderm, mesoderm and endoderm all demand vitamins . . . Although each vitamin does not affect only one structure, yet it appears that each vitamin has a special relation to one germ layer." Vitamin

23. Mellanby, E.: Vitamin A and Bone Growth: Reversibility of Deficiency Changes, J. Physiol. **105**:382 (Jan.) 1947.

24. Wolbach, S. B., and Bessey, O. A.: Relative Overgrowth of the Central Nervous System in Vitamin A Deficiency in Young Rats: Explanation of Neurological Lesions Occurring in This Deficiency, Science **91**:599 (June 21) 1940.

25. Loch, W. E.: Veränderungen der Labyrinthkapsel bei tierexperimentellen Avitminosen (A, C, D, E), Monatsschr. Ohrenh. **73**:542 (Aug.) 1939.

26. Perlman, H. B., and Willard, J.: The Ear in Experimental Vitamin A Deficiency, Ann. Otol., Rhin. & Laryng. **50**:349 (June) 1941.

27. Evans, W. H.: Vitamins in Ophthalmology and Otolaryngology: A Review of Recent Experimental and Clinical Observations, Ohio M. J. **35**:944 (Sept.) 1939.

28. Baer, M.: Lässt sich die Otosklerose durch Vitamine beeinflussen? Schweiz. med. Wchnschr. **69**:1328 (Dec. 30) 1939; L'Oto-Sclérose est-elle influençable par les vitamines? Rev. laryng. **61**:33 (Jan.) 1940; Zur Vitaminbehandlung der Otosclerose, Monatsschr. Ohrenh. **74**: 113 (March) 1940.

29. Kubomura, M.: Ein geheilter Fall von Schwerhörigkeit durch Vitamin C, Oto-rhino-laryng. **12**:706, 1939.

30. Childrey, J. H.: Vitamin B and Other Measures in the Treatment of Deafness, Laryngoscope **50**:648 (July) 1940.

31. Jones, I. H.: Vitamins and the Ear, Nose and Throat, Laryngoscope **50**:585 (July) 1940; Vitamins and the Eye, Ear, Nose and Throat, ibid. **51**:609 (July) 1941.

A affects the ectoderm and endoderm; B complex, the ectoderm; C, the mesoderm (connective tissue), and D, the mesoderm (bone formation). Cochlear and vestibular epithelium and nervous structures of the internal ear are derived from ectoderm. Previously Wolbach and Howe [32] had observed in animals that vitamin A deficiency results in metaplasia of the ectodermal leaf and substitution of keratinized epithelium for stratified epithelium in the respiratory tract, ocular tract, paraocular glands and alimentary and genitourinary tracts.

On the negative side of the subject, Shambaugh [33] asserted that the strongest argument against the theory that vitamins are important in nerve deafness is the fact that deafness is not a symptom of clinical avitaminosis. Scurvy, beriberi and pellagra have not been shown to be associated with nerve deafness. Hughson and Thompson [34] pointed out that there is no more completely disappointing phase of the therapy of deafness than the supposed effect of vitamins on hearing. "From an anatomic standpoint alone, neural impairment of hearing is final and, in its manifest and individual degree, complete. Why should vitamin B or any one of its various complexes restore function to an organ of Corti deprived of its neural mechanism? . . . It is most unlikely that any of the neurologic effects produced by extreme experimental lacks are significant from the standpoint of human clinical deafness. All reported results of therapy are completely inconclusive. There is no anatomic evidence that the anatomic result of dietary difficulties is corrected by appropriate vitamin replacement. At the moment it would seem that this entire subject is lacking in true scientific control which is possible only with animal experimentation. Any human audiograms so far presented are of no real significance if taken as a measure of the effectiveness of vitamin therapy."

Despite these adverse opinions, there is substantial foundation for the belief that there is a relation between vitamins and deafness. Canfield [35] goes so far as to say that evidence from experiments on certain nerves indicates that damage caused by vitamin deficiency can be overcome by the therapeutic use of these substances. "It is now supposed that there is a pathologic stage in the cochlear mechanism in which the nerve elements lose part of their function without irreparable damage having been done . . . Enough people now have improved hearing following the administration of this group of vitamins (vitamin B complex) so that it must be considered as part of the therapeutic armamentarium of the physician at this stage of the experimental approach."

MY EXPERIMENTS

In the present study, vitamin A was selected for trial in the treatment of deafness for various reasons. It has been conceded in some quarters that cod liver oil is beneficial in certain types of deafness. In the case of animals it has been demonstrated that vitamin A was apparently the factor of cod liver oil that influenced the

32. Wolbach, S. B., and Howe, P. R.: Tissue Changes Following Deprivation of Fat-Soluble "A" Vitamins, J. Exper. Med. **42**:753 (Dec. 1) 1925.

33. Shambaugh, G. E., Jr.: Chronic Progressive Deafness, Including Otosclerosis and Diseases of the Inner Ear, Arch. Otolaryng. **33**:436 (March) 1941.

34. Hughson, W., and Thompson, E.: Otological Research and Its Recent Contributions to Clinical Otology, Ann. Otol., Rhin. & Laryng. **50**:77 (March) 1941.

35. Canfield, N.: The Therapy of Deafness, Internat. Clin. **1**:192 (March) 1941.

"wrong" bone growth of the periosteal capsule in otosclerosis.[36] From an embryologic standpoint, vitamin A should favorably affect the cochlear and vestibular epithelium and nerve structures of the internal ear, since they are derived from ectoderm. Moreover, as Dickie [37] pointed out, "It is unlikely that the deafness of otosclerosis is entirely due to the fixation of the stapes. The improvement following treatment with amyl nitrite could not be due to loosening the ankylosed stapes. More probably the deafness is due to lowering of the function of the neurons concerned with hearing."

Finally, recent studies with carotene and vitamin A have shown this nutrient to be of definite value in deafness. Hollender,[38] in his well known work, "Office Treatment of the Nose, Throat and Ear," refers to the good results Schillinger obtained with 100,000 units vitamin A administered daily by mouth, along with 20 growth units of anterior pituitary extract once a week. Kopetzky [39] recommended 25,000 units a day of carotene in oil, 4 grains (0.26 Gm.) yeast concentrate three times a day and anterior pituitary extract once a month. Of 97 patients receiving this therapy, 85.5 per cent showed an average hearing gain of 8.92 per cent and 13.4 per cent an average hearing loss of 9.22 per cent; in about 1 per cent of the patients the condition remained static. Hume and Krebs [40] reported on five persons deprived of vitamin A; of these, the conditions of three deteriorated through the further deprivation of vitamin A but subsequently improved significantly when vitamin A was added to the diet.

REPORT OF CASES

The following reports of cases have been selected from the histories of patients with varying degrees of hearing loss. These patients were treated primarily with vitamin A and other measures, as indicated and described.

CASE 1.—V. Z., a woman aged 40, had a chief complaint of impairment in hearing for the past nine years. She first became aware of a difficulty in hearing following an intermittent buzzing tinnitus which disappeared completely after three years. Her family history was not significant, and she stated she had had no previous otitic infections. Another otologist refused to perform a fenestration operation, prior to this consultation, for obvious reasons.

Examination revealed the septum of the nose deviated to the right, but aeration was adequate and there was no impairment. The nasal chambers were free of pus. The lingual tonsils were present; otherwise the throat showed nothing significant. In the right ear the canal was moderately wide and the cerumen scant. The drum membrane was translucent and the ossicles and membrane were movable. Cough and vascular reflexes were present. The left ear was essentially the same. The Rinne test was negative, the Schwabach test showed reduced bone conduction and in the Weber test sound lateralized to the right ear.

Results of functional tests with tuning forks were as follows: with a C fork the ratio of air conduction to bone conduction was 0/45 : 10/20 in the right ear and 17/45 : 5/20 in the

36. Mellanby, E.: Croonian Lecture: Nutrition in Relation to Bone Growth and the Nervous System, Proc. Roy Soc., London, s. B **132**:28 (March) 1944.

37. Dickie, J. K. M.: Progressive Deafness, Otosclerosis and Diseases of the Labyrinth: A Review of the Literature of 1928, Arch. Otolaryng. **9**:659 (June) 1929.

38. Hollender, A. R.: Office Treatment of the Nose, Throat and Ear, Chicago, The Year Book Publishers, Inc., 1943, p. 434.

39. Kopetzky, S. J.: Symposium: Progressive Deafness: Present Status of Medical and Surgical Therapy of Deafness, Laryngoscope, **54**:217 (May) 1944.

40. Hume, E. M., and Krebs, H. A.: Vitamin A Requirements of Human Adults: An Experimental Study of Vitamin A Deprivation in Man, London, His Majesty's Stationery Office, 1949, p. 124.

left; with a c 4 fork hearing was 0/45 in the right ear and 6/45 in the left. The lowest limit was a C 64 fork, which could be heard in the right ear by bone conduction only and in the left by air conduction and bone conduction.

Blood examination indicated high uric acid and high pyruvic acid levels. The albumin: globulin ratio was less than 2: 1.

The patient was referred back to her otologist with the recommendation that she be given anatola® parenterally twice weekly and high potency vitamin B complex therapy intravenously biweekly. The results of five weeks' therapy are indicated in chart 1 *A* and *B*.

Case 2.—L. F., a man aged 65, had a complaint of hearing loss for the past five years that had grown progressively worse. The onset, he stated, was gradual. He gave a usual history as to tinnitus, previous otitic infection and heredity. As a child he had measles and chickenpox, and he has recurrent yearly attacks of bronchitis.

Examination revealed the nasal chambers full of pus except over the superior concha, which showed the presence of a chronic ethmoiditis. The throat was essentially normal. In the right ear the canal was moderately wide and the cerumen present. The drum membrane was thickened and retracted; the cone of light was fragmented. The cough reflex was present and the vascular reflex slow. The drum membrane and ossicles were movable. In the left ear the canal was moderately wide and the cerumen present. The drum membrane was retracted and thickened; the cone of light was present. The cough and vascular reflexes were absent.

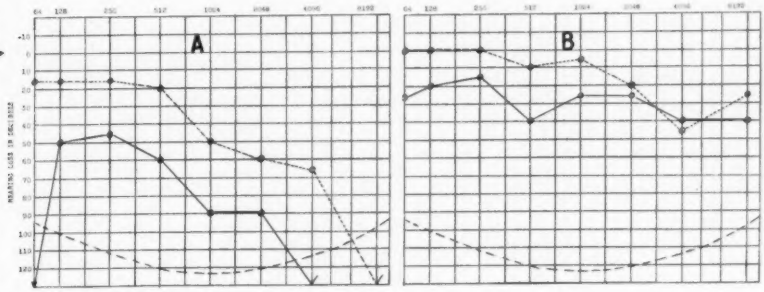

Chart 1.—Audiograms for V. Z. *A*, taken Sept. 8, 1949, before therapy; *B*, taken Dec. 15, 1949, shows the results of five week's therapy.

Movement of the drum membrane and ossicles was restricted. The Rinne test was negative, the Schwabach test showed reduced bone conduction and in the Weber test sound lateralized equally.

Results of functional tests with tuning forks were as follows: with a C fork the ratio of air conduction to bone conduction was 16/45: 5/20 in the right ear and 12/45: 0/20 in the left; with a c 4 fork hearing was 2/45 in the right ear and 0/45 in the left. The lowest limit was a C 64 fork, which could be heard in the right ear by air conduction and bone conduction and in the left by air conduction only.

Blood examination indicated a high pyruvic acid, low vitamin A, level and a reduced albumin: globulin ratio.

The ethmoiditis was treated, and the patient was given anatola® in 2 cc. doses intragluteally biweekly and vitamin B complex with a higher thiamin content intravenously twice a week. After two weeks of therapy, he was referred to his otologist with the recommendation for further continuance of therapy. Chart 2 *A* and *B* shows the results of therapy.

Case 3.—C. D., a man aged 46, had a chief complaint of very marked impairment in hearing for the past seven years. It was his belief that this marked hearing loss followed a severe cold and was becoming progressively worse. He also complained of frequent headaches and stated his mother had impaired hearing. There was an accompanying tinnitus resembling a waterfall in both ears. There was no paracusis Willisiana.

Examination revealed a bilateral ethmoiditis of the nose present at the time of examination, for which mild topical suction was used, and hydroxyamphetamine (paradrine®)-sulfathiazole nose drops to which 250,000 units of penicillin to 1 ounce (28.35 Gm.) was added, was prescribed. The throat showed nothing significant. In the right ear the drum membrane was perforated centrally, and occluding these perforated areas were small polypi. These polypi were touched with dichloracetic acid. Three weeks was permitted to elapse, and the hearing was checked audiometrically. The left ear was the same as the right. The Rinne test was negative, the Schwabach test showed reduced air and bone conduction and in the Weber test sound lateralized equally.

Chart 3*A* is the pretreatment audiogram; chart 3*B*, the audiogram secured following obliteration of evident aural polypi, indicates the level of hearing prior to use of anatola® parenterally, and chart 3*C* indicates the level of hearing following a course of therapy over a period of two weeks.

Case 4.—M. S., a woman aged 55, had chief complaints of difficulty in hearing for the past two years and intractable roaring tinnitus. She stated she heard better in a quiet room. She denied having any otitic infections but believed the impairment in hearing followed a severe cold. Her brother had impaired hearing. As a child she had typhoid; she had a tonsillectomy at the age of 25 and a panhysterectomy eight years before this paper was written.

Examination revealed that the nose was essentially normal. A large lingual tonsil was present on the left side of the throat. In the right ear the cerumen was scant, the canals

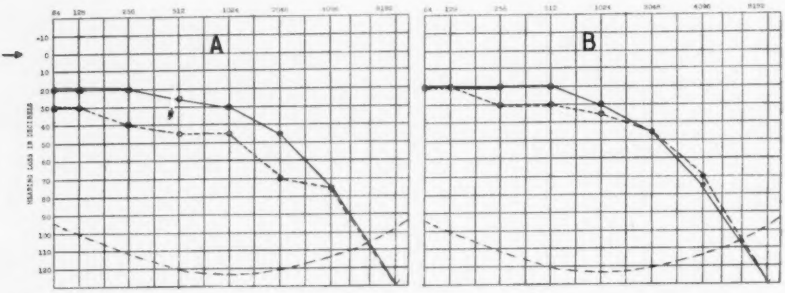

Chart 2.—Audiograms for L. F. *A*, taken April 22, 1949, before therapy; *B*, taken May 6, 1949, after two weeks of therapy.

moderately wide and the drum membrane retracted. The posterior portion of the membrane and ossicles was movable. The cough and vascular reflexes were absent. The left ear was the same as the right. The Rinne test was positive, the Schwabach test showed reduced bone conduction and in the Weber test sound lateralized equally.

Results of functional tests with tuning forks were as follows: with a C fork the ratio of air conduction to bone conduction was 8/45 : 6/20 in the right ear and 12/45 : 5/20 in the left; with a c 4 fork hearing was 10/45 in both the right and left ears. The lowest limit was a C 64 fork, which could be heard in the right ear by both air conduction and bone conduction and in the left by bone conduction only.

Blood examination revealed moderately low vitamin A and higher cholesterol levels.

The patient was referred back to her physician for therapy, with the recommendation of the administration of 2 cc. anatola® intragluteally biweekly. The patient was rechecked as to her hearing status five weeks later (chart 4 *A* and *B*).

Case 5.—M. G., a woman aged 46, was aware of an impairment in hearing for several years. This impairment had become particularly marked in the past year. There was no family history and no tinnitus, and she had several nonsuppurative ear infections in childhood. She could hear some persons clearly and some not at all. She had had the usual childhood diseases, measles and chickenpox, and a tumor of the ovary was removed in 1945.

Examination revealed nothing significant in the nose and throat. In the right ear the canal was moderately wide; the cerumen scant. The drum membrane and ossicles were movable, and the membrane was thin and translucent. Cough and vascular reflexes were absent. In

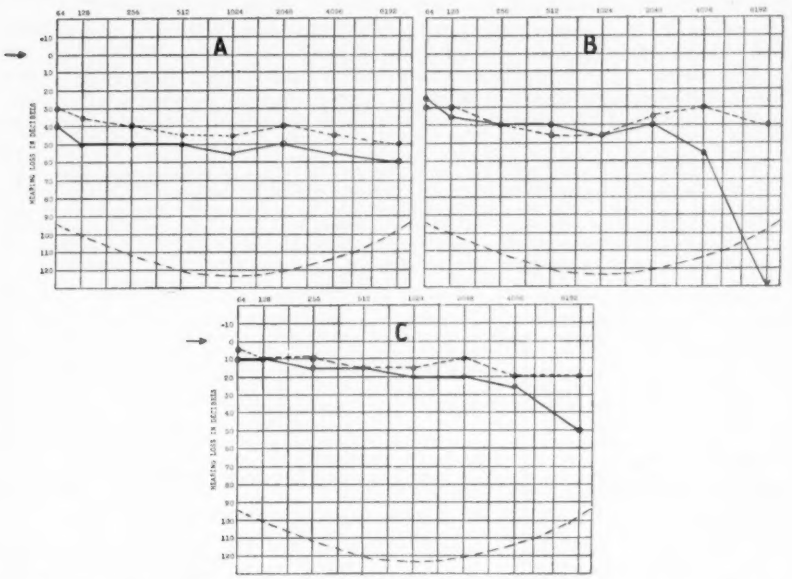

Chart 3.—Audiograms for C. D. *A*, taken May 26, 1949, before therapy, *B*, taken June 14, 1949, following obliteration of aural polypi and prior to use of anatola® and *C*, taken July 1, 1949, following a two week course of therapy.

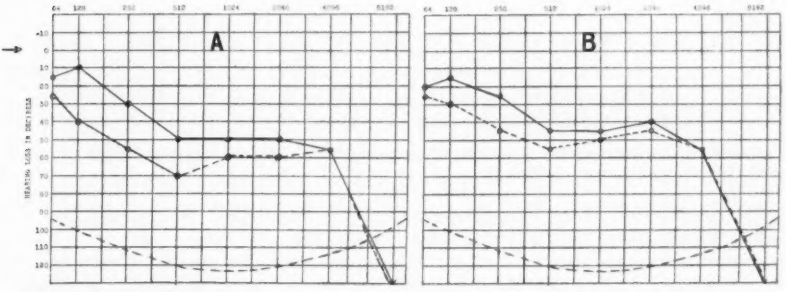

Chart 4.—Audiograms for M. S. *A*, taken Aug. 31, 1949, before therapy; *B*, taken Oct. 5, 1949, after five weeks of therapy.

the left ear the canal was moderately wide; the cerumen scant. Movement of the drum membrane and ossicles was restricted, and the membrane was thin and translucent. The cough reflex was absent and the vascular reflex present. The Rinne test was positive, the Schwabach test showed reduced bone conduction and in the Weber test sound lateralized equally.

Results of functional tests with tuning forks were as follows: with a C fork the ratio of air conduction to bone conduction was 8/45 : 7/20 in the right ear and 7/45 : 4/20 in the left; with a c 4 fork hearing was 8/45 in the right ear and 3/45 in the left.

Blood examination indicated high cholesterol and low vitamin A levels. Therapy with anatola® administered parenterally was instituted for eight months (chart 5 *A* and *B*).

CASE 6.—M. H., a woman aged 52, had a history of impaired hearing for over 25 years which had its onset following a profound shock. Hearing seemed worse after excitement and in damp weather. Her family history showed that her grandfather and mother had severe impairment in hearing. There was no history of otitic infections and tinnitus. As a child she had measles and whooping cough and as an adult, chickenpox, and scarlet fever. She

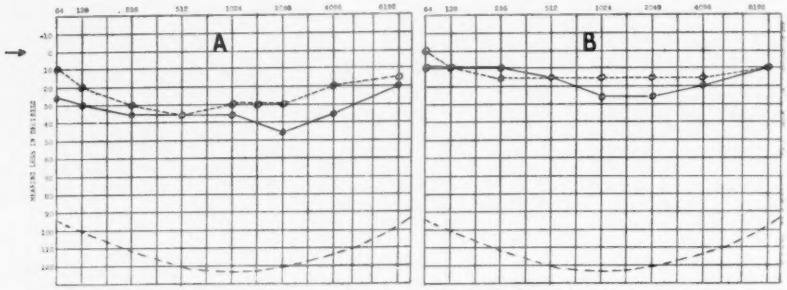

Chart 5.—Audiograms for M. G. *A*, taken March 10, 1949, before therapy; *B*, taken Nov. 3, 1949, after eight months of therapy.

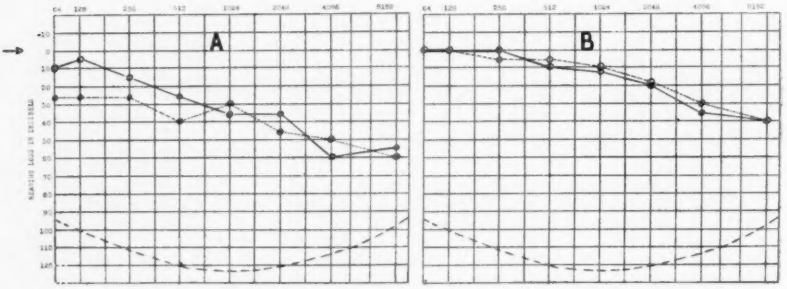

Chart 6.—Audiograms for M. H. *A*, taken Jan. 6, 1946, before therapy; *B*, taken March 20, 1947, after administration of therapy.

had pneumonia 14 years ago, occasional sinusitis and a tonsillectomy 18 years ago. She consulted otologists for a fenestration operation but was refused.

Examination revealed a purulent discharge in the left middle meatus of the nose. The tonsils had been removed, and the throat otherwise showed nothing significant. In the right ear the canal was wide and the cerumen absent. The drum membrane was thin and translucent. The cone of light was present. A blush was visible over the promontory. Movement of membrane and ossicles was restricted. The left ear was essentially the same as the right. The Rinne test was positive, the Schwabach test showed reduced bone conduction and in the Weber test sound lateralized equally.

Results of functional tests with tuning forks were as follows: with a C fork the ratio of air conduction to bone conduction was 12/45 : 10/20 in the right ear and 17/45 : 12/20 in the left; with a c 4 fork hearing was 8/45 in the right ear and 10/45 in the left.

Blood examination indicated a relatively low vitamin A value and a high pyruvic acid level. There was evidence of hypoproteinemia.

Treatment was directed toward improving the dietary habits. Anatola® was administered parenterally biweekly. High potency vitamin B complex therapy was given intravenously. Chart 6 *A* and *B* shows the results of therapy. The sinusitis was treated by mild capillary suction and administration of penicillin aerosol.

COMMENT ON STUDIES

The incidence of tinnitus accompanying loss of hearing acuity in Bright's disease and in cirrhosis of the liver prompted me, as long ago as 1942, to order blood studies made on all patients with symptoms of deafness, tinnitus and vertigo. Kopetzky [39] drew attention to my studies in an article which he published in 1944. A definite pattern was pursued; determination of nonprotein nitrogen, urea, uric acid, total proteins, glucose, cholesterol, calcium, carotene, vitamin A, vitamin B as pyruvic acid, albumin, globulin and in indicated cases alkaline phosphatase. In the absence of jaundice, in those patients exhibiting a low serum albumen, a sulfobromophthalein test was performed to estimate the amount of dye retained by the liver as evidence of chronic parenchymal damage and consequent poor liver function. In these patients intensive vitamin B complex therapy produced either a very definite amelioration of symptoms or a complete disappearance of those referable to the ear.

The patients presenting hypercholesteremia together with an elevated alkaline phosphatase level showed the presence of an intrahepatic obstruction. Hypercholesteremia was a variable finding in many cases. Blood serum levels varied from month to month. Intestinal spasm frequently gave higher cholesterol readings of 400 to 450. Administration of a cholagogue and antispasmodic would serve to reduce the cholesterol to approximately normal. These tests, however, impose certain limitations, and frequently the otologist must drift far afield from his specialty in the diagnosis of these specific cases.

The difficulties encountered in the absorption and utilization of carotene from the digestive tract together with the additional work imposed on the liver in the conversion of carotene into two molecules of vitamin A were realized, and a preparation for parenteral administration was developed [1] whereby absorption from the gastrointestinal tract would be by-passed and the available vitamin A would exert a pharmacological as well as a therapeutic response. Results in 300 patients on whom this therapy was used indicated an average gain of hearing in the left ear of 18.9 per cent and in the right ear of 17.3 per cent. Fifty-one patients failed to benefit from the treatment. Two hundred and forty-nine patients showed very definite gains in hearing of conversational tones. Amelioration and cessation of tinnitus occurred in the same proportions.

A study was started over 10 years ago on the empirical use of carotene in the treatment of deaf persons. Results in 100 patients indicated 33 per cent showed a gain of between 20 and 40 decibels; 47 per cent showed equivocal results, with gains of 10 decibels on one audiometric chart and reversion to pretreatment levels in the ensuing chart, and 20 per cent indicated either no result or further recession in hearing acuity. After four to six months, none of the above gains was sustained and the hearing returned to pretreatment levels.

An attempt was then made to combine the administration of vitamin B complex and carotene in an effort to maintain the gain in hearing. The result did not show improvement over that of the carotene therapy itself. The body apparently could utilize carotene up to a point at which a therapeutic effect was established, but the pharmacological result was lacking. Hepatic disorders [41] could (*a*) influence the absorption and the emulsification of fats, and consequently of the provitamin A, (*b*) interfere with the absorption of calcium and iron and (*c*) cause a precipitation of cholesterol and fatty acids.

A significant finding in patients complaining of deafness or of deafness and tinnitus solely and not as complications of systemic disease was the usual lower level of vitamin A. If, however, a lowered vitamin A level was associated with the finding of a higher cholesterol level as well as increased pyruvic acid, then the administration of vitamin A and vitamin B complex produced a very rapid increase in hearing levels. In those patients showing normal blood chemical levels, response to vitamin A therapy alone resulted in appreciable gains in 30 per cent of the patients under study, but the treatment time schedule was protracted.

CONCLUSIONS

The findings of Mellanby and other investigators seem to support the theory that deafness is a nutritional deficiency disease. The present clinical study likewise seems to confirm the views held by some workers that vitamin deficiency and hearing loss are in some manner related.

Results of clinical trials with a new injectable vitamin A preparation hold out promise of its therapeutic value in certain types of deafness. Despite the fact that in some instances the hearing loss was not influenced, the accompanying tinnitus was greatly relieved.

The necessity of a comprehensive physical examination of every patient is stressed. Examination should also include every pertinent laboratory test.

From the results thus far obtained by me and by other workers in the treatment of hearing loss, further trials with vitamin A, alone or combined with other vitamins, seem definitely warranted.

25 West Fifty-Fourth Street (19).

41. Teeter, E. J.: Bile Physiology and Therapy, J. A. M. A. **131**:1482 (Aug. 31) 1946.

SECONDARY TONSILLAR AND ADENOID HEMORRHAGE IN RELATION TO BAROMETRIC PRESSURE CHANGES

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AND
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DELAYED or secondary hemorrhage from the healing tonsillar fossa and adenoid site occurs relatively commonly. In the presence of known vascular or hematologic disorders the mechanism is usually apparent. In otherwise healthy persons the occurrence during the healing by secondary intention has been variously reported between 5.0 and 10.0 per cent.[1] The hypoprothrombinemic state caused by acetylsalicylic acid administration was carefully studied by Neivert and associates.[2] However, the counteractive effects of vitamin K and the supplemental administration of vitamin C have resulted in the reduction but not the elimination of secondary hemorrhage. This was anticipated by Neivert, as such added factors as trauma, menstruation, pregnancy, nutritional deficiency, dyscrasia and infection were considered as contributory causes.

The effects of weather on normal and on abnormal states have been postulated and correlated from the times of Hippocrates. Further studies have been made in relation to many body functions, the most extensive being that of Petersen.[3] The general aspects and a summary of such considerations are presented by Lederer.[4]

In the present study, evaluation is made of the time of occurrence of secondary tonsillar and adenoid site bleeding with respect to specific barometric changes, as on occasion it had been observed that almost simultaneous occurrence of secondary bleeding may exist in several persons.

METHODS

The cases observed represent those of 1,035 consecutive tonsillectomy and/or adenoidectomy patients observed over a three year period. It was attempted to reduce variables by limiting the study to children (ages 3½ to 13 years) with surgery performed with the patient under general anesthesia (vinyl ether induction and ether vapor maintenance); surgery was per-

From the Department of Otolaryngology, Michael Reese Hospital.

1. Singer, R.: Acetylsalicylic Acid: A Probable Cause for Secondary Post-Tonsillectomy Hemorrhage; Preliminary Report, Arch. Otolaryng. **42**:19-20 (July) 1945.

2. Neivert, H.: Late Secondary Tonsillar Hemorrhage: Studies of Prothrombin and Vitamin K, Arch. Otolaryng. **42**:14-18 (July) 1945.

3. Petersen, W. F., and Milliken, M. E.: The Patient and the Weather, Ann Arbor, Mich., Edwards Brothers, Inc., 1937.

4. Lederer, F. L.: Diseases of the Ear, Nose and Throat: Principles and Practice of Otorhinolaryngology, ed. 5, Philadelphia, F. A. Davis Company, 1946, p. 831.

formed by one surgeon employing a sharp dissection and snare technique for the tonsillectomy and using the LaForce adenotome, supplemented by use of biting forceps, under direct vision by means of retraction of the soft palate for the removal of the adenoid. Hemostasis was established primarily by suture or moderate pressure, occasionally by astringents. The 24 hour period following surgery was termed the first postoperative day, and succeeding 24 hour periods were successively numbered thereafter.

A Taylor aneroid barometer ("cyclo-stormograph") of the recording type was employed after calibration against mercury barometers and comparison with local reported barographic readings of the United States Weather Bureau. The instrument used was found to be accurate within ± 0.01 inch (0.0254 cm.). United States Weather Bureau reports were employed for information concerning relative humidity, hourly temperature, precipitation and wind velocity.

Preoperative bleeding and clotting times were within normal ranges. Postoperative medication for pain consisted of a combination of acetylsalicylic acid (0.33 Gm.), ascorbic acid (33.3 mg.) and menadione (0.33 mg.), which was administered only if needed.

Postoperative bleeding was considered to exist when any degree of bloody sputum or hematemesis was reported, and examination was made to determine whether or not hemostatic measures were required. The time of onset was recorded.

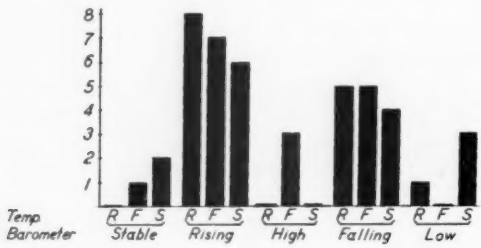

Chart 1.—Numbers of cases in which bleeding occurred and their individual correlation with temperature rising, falling and stable conditions and barometric pressure prevailing.

RESULTS

Forty-five cases of secondary tonsillar or adenoid site bleeding were observed in 1,035 consecutive cases (4.347 per cent), the first 24 hours after operation. The time and postoperative day were recorded and correlated with barometric pressure and prevailing outdoor temperature. The random occurrence in relation to reported relative humidity, wind direction and velocity and precipitation indicated that no direct relation of these factors could be correlated with bleeding. This was anticipated in view of the fact that these factors are most readily altered in the patient's environment by indoor confinement.

Either temperature or barometric pressure was considered "stable" if there was no recorded change in the two hours prior to the onset of bleeding. A "high" barometric crest was considered to exist when there was a rapid change in pressure from a previous rise to a fall; likewise, a "low" trough was considered to exist at the point of change from a previous fall to a sudden rise. Thus 15 combinations of temperature and pressure were considered: a rising, falling or stable temperature coupled with barometric stability, rise, "high," fall or "low." Each of the 45 postoperative instances of bleeding was classified in one of these categories; the results are presented in chart 1. Considering these data in relation to percentage, 6, 7 and

9 per cent occurred when barometric pressure was stable, "high" or "low," respectively, while 30 per cent occurred with a falling barometric pressure and 46 per cent with rising pressure.

Bleeding was observed as early as the third postoperative day but not later than the eighth day. Accordingly, 20 per cent occurred on the fifth, 28.8 per cent on both sixth and seventh postoperative days; 77.7 per cent of the total occurred on the fifth, sixth and seventh days as shown in chart 2. The tonsil fossa was the bleeding site in 84.5 per cent; the nasopharynx, in 15.5 per cent.

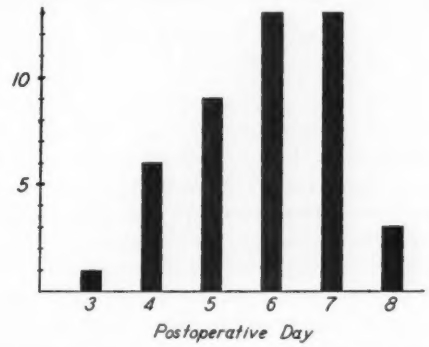

Chart 2.—Relation of cases of hemorrhage to postoperative time of occurrence. The 24 hours immediately following surgery is considered the first postoperative day.

SUMMARY AND CONCLUSIONS

Delayed secondary hemorrhage occurred in 4.347 per cent of 1,035 consecutive tonsillectomies and adenoidectomies performed on children under general anesthesia. Preoperative bleeding and clotting times were within normal limits. When acetylsalicylic acid was given postoperatively, it was in combination with ascorbic acid and vitamin K. In the three year period of observation, 77.7 per cent of bleeding occurred on the fifth, sixth and seventh postoperative days; 30 per cent occurred with a falling barometric pressure, and 46 per cent occurred with rising pressure.

It is not concluded that temperature and pressure conditions cause postoperative tonsil and adenoid site bleeding, but on the basis of the reported findings it is conceivable that the time of occurrence may be altered by prevailing conditions of these factors.

55 East Washington Street.

104 South Michigan Avenue.

TREATMENT OF COMPLETE UNILATERAL BONY ATRESIA OF THE POSTERIOR NARES

A New Technique and a Brief Reference to Asphyxia Neonatorum

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BROOKLYN

THE PURPOSE of this paper is to describe an approach, different from any thus far employed, in the treatment of a case of unilateral bony atresia of the posterior nares. This procedure is comparatively simple. It is not destructive to the extent that normal structures are sacrificed to attain a proper result and it enables covering the bare bony surface with mucous membrane to prevent the closure of the newly formed opening. The nasal and pharyngeal mucous membranes covering the bony atresia are utilized to cover the bare bony rim of the posterior nares after the bony atresia has been removed. The entire operative field can be clearly visualized because proper exposure is obtained. The same technique can also be applied in cases of bilateral atresia. In cases in which a deviated septum is obstructing, a submucus resection can be combined with this procedure. It is not recommended for choanal atresias in infants. The procedure also maintains the normal anatomical relation of the adjacent nasal structures.

ATRESIA OF THE POSTERIOR NARES

Statistics.—Atresia of the posterior nares, a congenital anomaly, is considered to be rather uncommon. Kazanjian [1] gives figures to prove the rarity of choanal atresia. He stated that in the records of the Massachusetts Eye and Ear Infirmary from 1922 to 1938 he found 10 cases of postnasal atresia from a total of 62,228 cases. Cinelli [2] found 220 cases reported in the literature for the 90 years previous to 1940, or an average of about 2½ cases a year. From then to the end of 1949, I found 54 additional cases reported in the American literature, an average of six cases a year. These figures prove that cases of postnasal atresia are being recognized more frequently now and may not be so uncommon as was formerly thought

Many more cases could be listed if the important work of Ronaldson [3] is taken into consideration. As far back as 1881, he described a case of bilateral membranous atresia, which he recognized clinically in an infant. Operation was delayed, and

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Read before the Section on Laryngology, Rhinology and Otology of the Medical Society of the County of Kings and Academy of Medicine of Brooklyn, Inc., Brooklyn, Jan. 10, 1951.

1. Kazanjian, V. H.: The Treatment of Congenital Atresia of the Choanae, Ann. Otol., Rhin. & Laryng. **51**:704-711, 1942.

2. Cinelli, A. A.: Nasal Atresias: A Surgical Critique, Ann. Otol., Rhin. & Laryng. **49**:912-923, 1940.

3. Ronaldson, T. R.: Note on a Case of Congenital Closure of the Posterior Nares, Edinburgh M. J. **26**:1035, 1880-1881.

the baby died of asphyxia. He believes that many cases of asphyxia neonatorum are due to atresia of the posterior nares. He arrived at this conclusion from his work on infants whose deaths were diagnosed as caused by asphyxia neonatorum, and at autopsy he found that bilateral atresia was often present. Since this is a problem usually dealt with and as yet not fully recognized as a possibility by the obstetrician and pediatrician, the otolaryngologist is, therefore, never called to see these patients. A number of cases are therefore overlooked.

Pastore and Williams [4] stated that their youngest patient at the Mayo Clinic was 1 day old and the oldest was 34 years old. Most of the cases I reviewed were found to occur in patients from 11 to 20 years old. From a survey of the literature, more cases are found to appear in the female. Statistics have not as yet been accurately compiled, describing the number of bilateral atresias and the number that are of the unilateral type, which involves the right or the left naris and which is bony or membranous. Complete bony atresias seem to be the type most commonly described. Fraser,[5] however, in 1910 reviewed 115 cases and found 54 per cent of them to be unilateral, the right side involved in 62 per cent and 90 per cent of them bony.

Embryology.—Embryologically the exact explanation for this anomaly is still obscure. An explanation, however, is offered (Schaeffer,[6] Boyd [7] and Schwartz and Isaacs [8]) stating that congenital atresia of the choanae is believed to be due to the persistence of the bucconasal or nasopharyngeal membrane. This membrane separates the nasal fossa from the primitive oral cavity and ordinarily ruptures during the fifth or sixth week to produce the primitive choanae. When the bucconasal membrane fails to rupture, the atresia develops.

The bucconasal mucous membrane is formed by the nasal epithelium and pharyngeal epithelium with the mesoderm between them. The atresia is bony or membranous or both depending on how much of the mesoderm remains between the nasal and pharyngeal epithelium.

Boyd [7] shows some schematic drawings by Colver [9] of the embryological development of the posterior nares.

Anatomy.—Anatomically the roof of the posterior nares is formed by the alae of the vomer and the body of the sphenoid bone, while the floor is represented by the line of junction of the hard and soft palates (Donnelly [10]). The vomer, or posterior edge of the septum, forms the medial boundary, and the lateral walls are limited by the medial plates of the pterygoid processes of the sphenoid bone.

4. Pastore, P. N., and Williams, H. L.: Congenital Occlusion of the Nasal Choanae: Brief Review of 12 Cases, Proc. Staff Meet., Mayo Clin. **14**:625-627, 1939.

5. Fraser, J. S.: Congenital Atresia of the Choanae, Brit. M. J. **2**:1698-1701, 1910.

6. Schaeffer, J. P.: The Lateral Wall of the Cavum Nasi in Man, with Especial Reference to the Various Developmental Stages, Ann. Otol., Rhin. & Laryng. **20**:277-366, 1911.

7. Boyd, H. M. E.: Congenital Atresia of the Posterior Nares: Descriptions of Technics Used in Meeting Operative Difficulties and Report of Case, Arch. Otolaryng. **41**:261-271 (April) 1945.

8. Schwartz, A. A., and Isaacs, H. J.: Congenital Atresia of Posterior Nares: Report of 2 Cases, Arch. Otolaryng. **35**:603-612 (April) 1942.

9. Colver, B. N.: Congenital Choanal Atresia: Two Cases of Complete Bilateral Obstruction, Ann. Otol., Rhin. & Laryng. **46**:358-375, 1937.

10. Donnelly, J. C.: New Method of Operation for Congenital Atresia of the Posterior Nares, Arch. Otolaryng. **28**:112-125 (July) 1938.

Anomaly.—Other anomalies are often found together with occlusion of the posterior nares. Binnerts [11] described a double tragus on each ear of a patient. A congenital coloboma of the iris was reported by Thomasson [12] in his case, and Blair [13] mentioned the presence of a cleft palate.

Frequently other associated anomalous defects are also present with this condition. Stinson [14] and Kazanjian [1] made a point of this when they observed an asymmetry of the face in some instances. The case described here presented low grade mentality as well as asymmetry of the face. The right side of the face was more prominent than the left.

Heredity.—Some observers have attempted to show a hereditary background and tendency associated with congenital closure of the posterior nares. The heredity theory has been advanced by some observers, such as Lang,[15] who cited a case in which a boy 15, a sister 16 and the mother 35 had complete bony atresia on the right side. Stewart [16] reported bilateral atresia in two sisters and mentioned that the death of a brother in infancy from asphyxia was probably due to the same condition.

Historical Review.—The bibliographical review reveals the trial and error period through which this surgery has passed. Following are some of the important changes in technique in chronological order in the development of the operation for the correction of atresia of the posterior nares. The progress made from a crude technique in its early stages to the more advanced and scientific methods of the present is shown.

In 1829, this condition was first recognized at autopsy and described by Otto.[17] Emmert,[18] in 1853, clinically diagnosed and surgically treated the first case of bilateral atresia in a 7 year old boy, by using a trocar to puncture the atresia. In 1885, von Schröetter [19] created an opening by means of galvanocautery, which he combined with chemical cauterization. A hand drill was used for this purpose by Hubbell [20] in 1886.

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11. Binnerts, A.: Einseitige Choanalatresie bei einem Säugling von drei Monaten, Arch. f. Laryng. u. Rhin. **34**:324-326, 1921.

12. Thomasson, W. J.: Congenital Bony Occlusion of the Right Nasal Choana, Laryngoscope **25**:221-223, 1915.

13. Blair, V. P.: Congenital Atresia or Obstruction of the Nasal Air Passages, Ann. Otol., Rhin. & Laryng. **40**:1021-1035, 1931.

14. Stinson, W. D.: Osseous Atresia of the Posterior Choanae, Arch. Otolaryng. **15**:101-103 (Jan.) 1932.

15. Lang, J.: Über Choanenatresie (Heredität derselben), Monatschr. f. Ohrenh. **46**:970-1001, 1912; cited by Schwartz and Isaacs.[8]

16. Stewart, J. P.: Congenital Atresia of the Posterior Nares, Arch. Otolaryng. **13**:570-583 (April) 1931.

17. Otto, A. W.: Lehrbuch der pathologischen Anatomie des Menschen und der Thiere, Berlin, A. Rucher, 1830.

18. Emmert, C. F.: Lehrbuch der Chirurgie, Stuttgart, F. v. R. Dann, 1853.

19. von Schröetter: Über angeborenen knöchernen Verschluss der Choanen, Monatschr. f. Ohrenh. **19**:97-102, 1885; cited by Morgenstern, D. J.: Arch. Otolaryng. **31**:653-662 (April) 1940.

20. Hubbell, A. A.: Congenital Occlusion of the Posterior Nares, Buffalo M. & S. J. **26**:193-206, 1886.

Borse,[21] in 1907, employed a trocar, saw and chisel followed by the insertion of a rubber tube into the opening in a patient 22 years old. In 1908, Uffenorde [22] made an airway with the aid of a chisel and curet, dissecting a septal flap from the posterior part of the septum to be used to cover the raw bony surface. Katz, Preysing and Blumenfeld [23] in 1913, in addition to the chisel and curet, used a rongeur to remove the posterior end of the vomer. Richardson [24] in 1913 performed a submucous resection to approach the atresia and then removed the posterior one third of the septum, and White [25] in 1918 removed the posterior end of the septum together with the atresia. Bonham [26] cites Rogers' observation in 1922 of an opening in one patient that was so small it produced a whistling sound when the patient breathed.

Blair [13] in 1931 and Ruddy [27] and Klaff [28] in 1945 approached the atresia through a transpalatine route. Stinson [14] in 1932 removed a part of the vomer in a girl 14 years old, permitting the right naris to communicate and drain into the left naris. Colver [9] in 1937 reported difficulty in maintaining the patency of the newly created choanae. To prevent the closure of the opening, Blair [13] in 1931 introduced the use of a split skin graft which was wrapped around a catheter and inserted into the opening. In 1938, Donnelly [10] sutured a full thickness graft to a no. 18 catheter and placed it through the newly created opening which he made by perforating the bony atresia and then enlarging the opening with a small biting forceps and a curet. In 1939, Kelly [29] used a chisel and sphenoid punch to remove the posterior edge of the septum at the same time the opening was created in a woman 20 years old. Morgenstern [30] in 1940 recommended that electrocoagulation be used once a week for eight weeks.

Kazanjian,[1] in 1942, described a rather intricate operation. He made an incision through the base of the columella which was carried along the floor of the nose going through and through the entire cartilaginous septum and parallel to the vomer up to the perpendicular plate of the ethmoid bone. He then carried it upward to the nasal dorsum. The bony septum with its membranous covering which was left was then removed and the atresia perforated with a chisel. The

21. Borse, cited by Bonham, W. L.: South. M. J. **35**:252-256, 1942.

22. Uffenorde, W.: Ein Fall von Choanalatresie mit Demonstration, Ztschr. Laryng., Rhin. & Otol. **1**:475-477, 1908.

23. Katz, L.; Preysing, H., and Blumenfeld, F.: Handbuch der speziellen Chirugie, des Ohres und der oberen Luftwege, Leipzig, Curt Kabitzach, 1911-1913, vol. 3, p. 432; cited by Cinelli.[2]

24. Richardson, C. W.: Congenital Occlusion of the Post-Nasal Orifices, with Report of a Case, Tr. Am. Laryng. A. **35**:226, 1913.

25. White, L. E.: An Operation for Bony Occlusion of the Posterior Nares, Laryngoscope **28**:571-583, 1918.

26. Bonham, W. L.: Congenital Choanal Occlusion, South M. J. **35**:252-256, 1942.

27. Ruddy, L. W.: A Transpalatine Operation for Congenital Atresia in the Small Child or the Infant, Arch. Otolaryng. **41**:432-438 (June) 1945.

28. Klaff, D. D.: Bilateral Congenital Atresia of the Choanae, Arch. Otolaryng. **41**:298-299 (April) 1945.

29. Kelly, D. B.: Congenital Occlusion of the Posterior Nasal Choanae, Brit. M. J. **1**:157-158, 1939.

30. Morgenstern, D. J.: Congenital Atresia of the Postnasal Orifices: Simple, Effective Office Technic for Treatment by Electrocoagulation, Arch. Otolaryng. **31**:653-662 (April) 1940.

nose was then packed with rubber finger cot plugs for 24 hours. Good results with this technique have been reported by Beyer and Blair.[31]

In 1942 Bonham [26] performed a submucous resection on a 25 year old woman for a complete unilateral bony occlusion. He then elevated the mucous membrane laterally over the anterior wall of the choanal occlusion. The occlusion was then removed with biting and punch forceps followed by the removal of one-half inch of the membranous septum. Roberts [32] in 1944 modified Bonham's [26] procedure by removing the posterior part of the vomer with a small mastoid gouge. The membrane was then split, and through it he inserted a no. 18 catheter.

Boyd [7] in 1945 excised the posterior third of septal soft tissue after doing a submucous resection with the removal of the vomer and with the placement of a plug in each choanal area. Wright, Shambaugh and Green [33] in 1947 described an approach by the transantral route used on a woman 23 years old for atresia of the left naris. Shearer [34] in 1947 vulcanized the end of a catheter which was pulled into position from the nasopharynx, the other end of the catheter extending out of the nose and fastened there. Durward, Lord and Polson [35] wrote a very thorough and detailed article on this subject. It is an excellent treatise and reference work on choanal atresia which is worth while reading.

From a description of the above reports of cases, one is impressed with the difficulty encountered in approaching the posterior nares as well as with the greater difficulty in maintaining a permanent opening. Many methods have been advanced, all of which sacrifice normal tissue, such as the septum, partially or in its entirety, together with the removal of part of the vomer and with the destruction of the nasal and pharyngeal mucous membrane of the bony atresia. An approach by way of the palate and the antrum has also been described.

All the above mentioned procedures create as their final result an artificial opening. This is accomplished at the expense of the surrounding structures and at the same time involving a great deal of surgical treatment.

Skin grafting and mucous membrane flaps have been used to line the newly created bony opening. The technique employed, in the cases in which it was tried, was not entirely satisfactory or practical. This attempt at skin grafting was performed in accordance with the surgical principle that all bony openings must be covered with tissue to prevent them from closing and thus to maintain their patency. After a review of the literature the only conclusion one can draw is that the treatment for atresia of the posterior nares is still not standardized.

Summary of Instruments and Methods Employed.—The first attempt at making an opening in the posterior nares was made with a trocar; this was followed by the use of the galvanocautery, chemical cauterization, the hand drill, chisel and curet. As the technique improved, a septal flap was created; the removal of the posterior end of the vomer with a rongeur was then performed. This was later followed by performing a submucous resection with the removal of the posterior third of the septum. A transpalatine approach was described and the vomer alone was removed.

31. Beyer, T. E., and Blair, J. R.: Choanal Atresia, Laryngoscope **57**:719-721, 1947.

32. Roberts, G. J.: Congenital Choanal Atresia, U. S. Nav. M. Bull. **43**:1216-1219, 1944.

33. Wright, W. K.; Shambaugh, G. E., Jr., and Green, L.: Congenital Choanal Atresia: A New Surgical Approach, Ann. Otol., Rhin. & Laryng. **56**:120-126, 1947.

34. Shearer, W. L.: Atresia or Stenosis of the Nares, Nebraska State M. J. **32**:116, 1947.

35. Durward, A.; Lord, O. C., and Polson, C. J.: Congenital Choanal Atresia, J. Laryng. & Otol. **60**:461-500, 1945.

A split skin graft wrapped around a catheter and inserted into the opening was used, then a full thickness graft on a catheter after perforation of the atresia. A sphenoid punch was used to remove the posterior edge of the septum at the time an opening was created. Electrocoagulation was tried. The perpendicular plate of the ethmoid bone was removed after perforation of the atresia with a chisel. The mucous membrane over the anterior surface of the atresia was elevated after a submucous resection was done, and its elevation was followed by the removal of one-half inch of the membranous septum. The posterior part of the vomer was removed and the mucous membrane split, through which a no. 18 catheter was inserted. A submucous resection with the removal of the vomer and posterior third of the septal soft tissue was done. An approach by way of the antrum was described; the end of a catheter was vulcanized and placed into the opening.

Symptoms.—In the adult, symptoms are primarily those of persistent nasal obstruction usually associated with a thick mucoid discharge. Any other associated symptoms may be only incidental.

In the newborn, one must bear in mind the possibility of bilateral posterior nasal atresia in all cases of asphyxia neonatorum. In unilateral atresia asphyxia is less evident but nevertheless should be thought of, especially in infants who have difficulty in breathing or nursing.

Diagnosis.—The diagnosis is simple and purely academic. If, after a careful examination of the interior of the nose no apparent cause is found to account for the nasal obstruction, a probe, catheter or other instrument should be used to determine the presence or absence of patency of the posterior nares. This can be further verified and confirmed by x-ray studies with iodized oil U. S. P. (lipiodol®). The postnasal mirror should also be used to see the posterior nares.

We have all heard stories of infants who suddenly died in their cribs with the explanation that they smothered to death from the blanket. Such deaths may have been due to an unrecognized unilateral atresia of the posterior nares.

REPORT OF A CASE

The following case is being reported, first because of its academic interest and second to describe a simple, logical and natural approach toward correcting an atresia of the posterior nares.

A procedure for maintaining a permanent patent posterior nares with a minimum amount of surgery and with the preservation of the normal anatomical relations is also described.

History.—A. P., a girl aged 16, had a chief complaint of nasal obstruction on the right with discharge since birth. The mother stated that at birth the patient acted like a child with a cold. She gulped her bottle, stopped, opened her mouth and gasped for air. This continued during the entire nursing period. When 4 months old she was treated for pneumonia and a discharging right ear. At the age of 3 years she was hospitalized for an acute purulent otitis media of the right ear. Tonsils and adenoids were removed at 7 years of age. On entering school she was referred to the child guidance clinic, where she was graded as mentally retarded. She is now in the third grade. There is no history of anyone else in the family having this condition.

Physical examination revealed a short, white, expressionless girl, well nourished and apparently comfortable. There was a marked facial asymmetry, the right side being more prominent than the left. The eyes and ears showed nothing significant. Tonsils and uvula were absent. Examination of the heart, lungs, blood and urine showed no pertinent findings.

A thick mucoid discharge completely filled the right nostril. After its removal, the right inferior turbinate bone was found to be pale and markedly edematous with enlargement of the posterior tip. The septum was not obstructive. A probe could not be passed into the nasopharynx through the right naris. Examination with the postnasal mirror revealed a normal left posterior

naris with complete closure of the right posterior naris. On palpation the occlusion of the right posterior naris was felt to be bony. The palate was highly arched.

X-ray examination with iodized oil U. S. P. confirmed the obstruction of the right posterior naris. The right maxillary sinus was smaller and situated higher than the left.

The diagnosis was congenital atresia of the right posterior naris.

Operation.—The operation was performed Nov. 1, 1950, at Long Island College Hospital.

After packing the right naris with equal parts of 10 per cent cocaine and epinephrine solution 1:1,000, the nasal mucous membrane on the floor of the nose and the septum were infiltrated with solution butethamine (monocaine®) 1.5 per cent with epinephrine 1:30,000 (Novocol Chemical Mfg. Co., Inc.). A sufficient amount of the solution was introduced to elevate the mucoperiosteum. The large posterior tip of the inferior turbinate bone together with the redundant mucous membrane was removed. The inferior turbinate bone was then fractured upward, thus increasing the amount of room in the lower half of the nose. An incision was then made

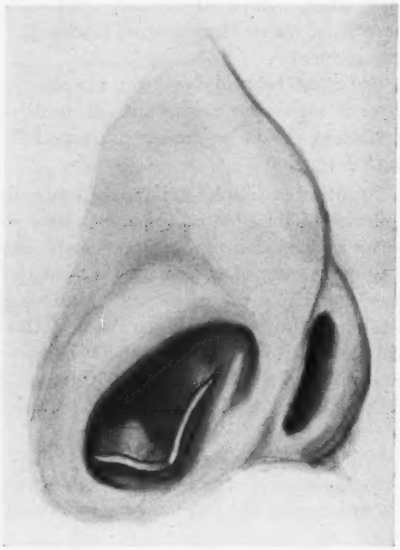

Fig. 1.—The incision is made down to the bone of the maxilla, just inside its anterior margin, on the floor of the nose, extending from the outermost lateral margin, carried along the floor of the nose to the septum and ends half way up the septum.

down to the bone of the maxilla, just inside its anterior margin, on the floor of the naris, extending from the outermost lateral margin and carried along the floor of the nose to the septum and then half way up the septum. With a sharp periosteal elevator the mucoperiosteum on the floor of the nose and the septum was elevated all the way back to the atresia. This elevation created a space sufficiently large to introduce a Killian nasal speculum. The mucoperiosteum in front of the atresia was now elevated in all directions. The bony atresia of the posterior naris was thus exposed and seen. The bony atresia was found to be convex from below upward, with the greatest convexity at its upper portion, and also convex from side to side. A defect was felt near the floor adjoining the septum. This defect was about 1 mm. in diameter. Starting at the floor and working laterally, superiorly and medially the bony atresia was removed with a 10 mm. gouge. The pharyngeal mucous membrane was not penetrated but seemed to be pushed backward by the gouge. The elevated mucoperiosteum was then replaced on the floor in its former position.

With a no. 11 Bard-Parker blade a stellate incision was made in the nasal mucous membrane of the atresial opening. A piece of heavy rubber tubing, 1 cm. in diameter, was inserted into the naris and passed through the opening made in the nasal mucous membrane. At this point there was difficulty in reaching the nasopharynx past the pharyngeal mucous membrane to which the button of bone was attached. A small esophageal bougie was then used as a guide and was passed into the nasopharynx, going through the defect on the floor of the nose. The bougie was brought from the nasopharynx out of the mouth, leaving the other end extending outside the nostril. The original piece of rubber tubing was now sutured with heavy silk to the nasal end of the bougie. The bougie was then pulled out of the mouth, carrying the rubber tubing into the nasopharynx and tearing the pharyngeal mucous membrane from its bony attachment.

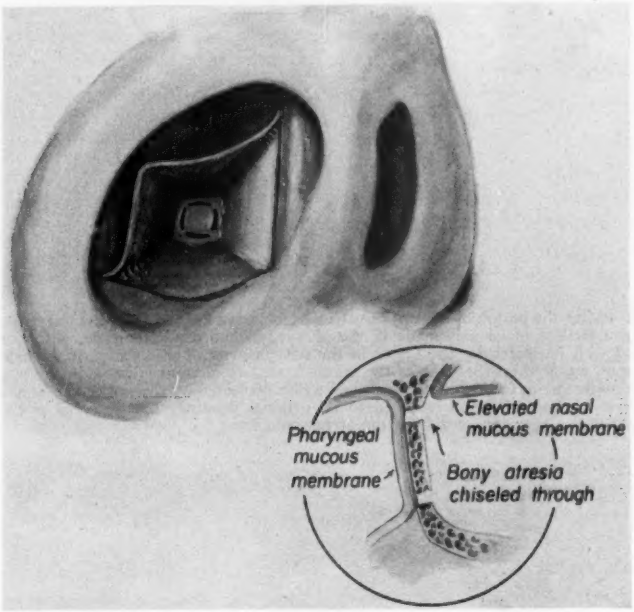

Fig. 2.—The inferior turbinate bone is fractured upward. The mucoperiosteum is elevated from the floor and septum to the bony atresia, exposing it and showing the bone chiseled through. The insert is the button of bone of the atresia separated from its attachment and freed from the nasal mucous membrane but still attached to pharyngeal mucous membrane.

The rubber tubing extended into the nasopharynx, ending just above the level of the soft palate. The tubing was made secure by passing a black silk suture through it and the membranous septum. The inferior turbinate bone was turned down to its former position before the nasal tube was passed. No other dressings were used.

Explanatory Comments.—The passage of the piece of rubber tubing into the nasopharynx caused the incised ends of the nasal mucous membrane to be reflected backward, thereby covering and lining the bare bony newly created choanal opening. The torn remnants of the posterior pharyngeal mucous membrane also aided in covering the atresia opening by uniting and healing together with the incised nasal mucous membrane. We thus have two membranes with raw surfaces facing each other to utilize to cover the bare bone, when either one alone would serve the purpose to maintain a permanent opening.

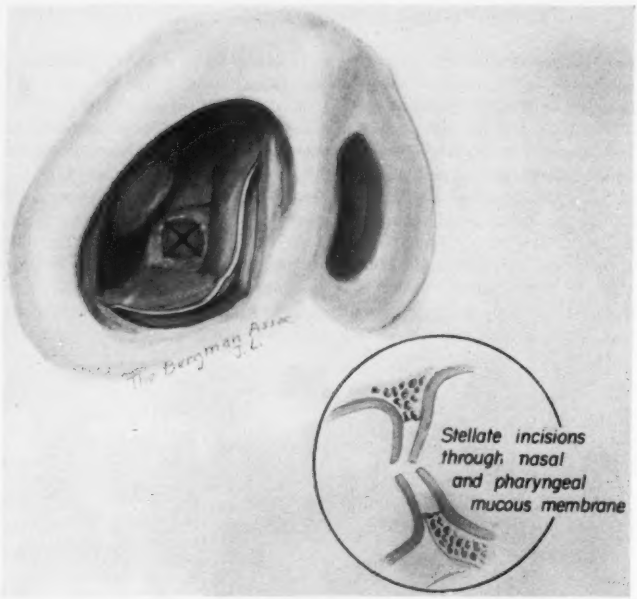

Fig. 3.—After the button of bone of the atresia has been removed from the pharyngeal mucous membrane a stellate incision is made in the pharyngeal mucous membrane, with the posterior pharyngeal wall protected by the finger in the nasopharynx. The elevated nasal mucous membrane is then replaced on the floor of the naris. A stellate incision is made in the nasal mucous membrane, with the posterior pharyngeal wall again protected by the finger in the nasopharynx. The inferior turbinate bone is returned to its original position. The insert is a cross section after the bone has been removed from the atresia and from the posterior pharyngeal membrane.

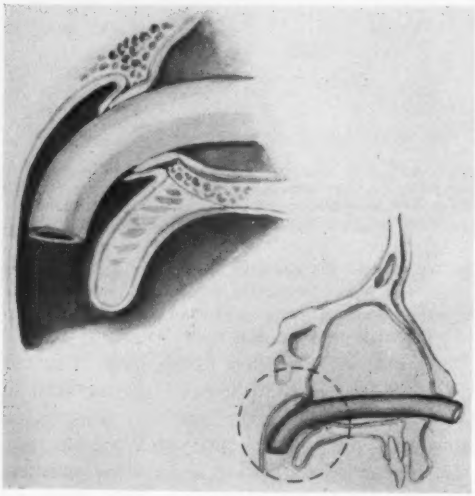

Fig. 4.—The incised nasal and pharyngeal mucous membranes are reflected backward over the bare bone with the raw surfaces facing each other and held in position by the rubber tubing which extends into the nasopharynx.

The presence of the rubber tubing through the opening in the posterior naris helps to maintain the fragments of mucous membrane in close contact to cover the bare bone. The firm pressure of the rubber tubing on the replaced mucous membrane on the floor of the nose and the septum prevents hemorrhage, eliminates any dead space and prevents the formation of a hematoma.

The size of the gouge used to remove the bony atresia is determined by the size of the anterior naris. The gouge should be large enough to fit snugly through the entrance of the nose. The posterior choana can be made larger than the anterior by using the nostril as a fulcrum. The size of rubber tubing to be inserted is determined in the same manner as the size of the gouge.

The suture in the membranous septum was removed on the third day, and the rubber tubing was removed at the end of the fifth day.

Critique.—In retrospect, the following suggestions are made.

The button of bone which was chiseled from the atresia and which remained attached to the pharyngeal mucous membrane should be removed. An incision could then be made in the pharyngeal mucous membrane, care being exercised to protect the posterior pharyngeal wall from injury by keeping the finger in the nasopharynx. This should be done before incising the nasal mucous membrane.

Since the posterior naris is about two and a half times larger than the anterior naris, this relation can be maintained by inserting the proper size of rubber tubing into the newly formed posterior choana by way of the nasopharynx.

SUMMARY

The literature on atresia of the posterior nares has been reviewed, showing the evolution of the operation since 1853.

An operation is described which is simple, effective and nondestructive. General anesthesia is not necessary. The nasal mucous membrane in front of the atresia and the posterior pharyngeal membrane are utilized to cover completely the raw bony surface of the newly created natural opening to prevent secondary closure.

Mention is made of the possibility of atresia in the newborn, especially in cases of asphyxia neonatorum. The posterior nares should be included in the examination at autopsy, in every infant dying from asphyxia neonatorum. The operation is recommended for the older child or adult but not for the newborn.

A suggestion is made for a more careful examination of the nares in all cases of persistent nasal obstruction in which all other causes have been eliminated.

Although it is too early to evaluate the final result in this case, the principle of the operation is sound and should work out well. There had been no change in the size of the opening when the patient was last examined on April 7, 1951. The patency remained the same as it was after the removal of the rubber tubing.

760 Eastern Parkway (13).

Case Reports

FRACTURES OF THE PETROUS PYRAMID

Report of a Case with Histological Observations Eight Years After Injury

JOSEPH G. DRUSS, M.D.
NEW YORK

FRACTURES of the petrous pyramid are commonly classified as (1) longitudinal and (2) transverse. The longitudinal fractures have been encountered far more frequently than the transverse. This is well shown in the comprehensive clinical study by Grove.[1] He analyzed 211 cases of fracture of the skull including 162 cases of temporal bone fractures, of which 146 were longitudinal and 16 transverse.

Longitudinal fractures are characterized by a break through the tegmen tympani or antri and by injury to the tympanic membrane and often to the external auditory canal. There is usually free bleeding from the ear. The bony capsule of the labyrinth is seldom involved. The transverse fractures, on the other hand, are characterized chiefly by injuries to the inner ear and bony capsule. Hemorrhage into the inner ear and tearing of the seventh and eighth nerves are frequent accompaniments.

A third type to be considered, and one which is encountered relatively infrequently, is the combined longitudinal and transverse fracture of the petrosa. Grove's figures disclosed only 16 such cases of a total of 211 skull fractures, and Voss's [2] figures disclosed six cases of a total of 63.

Because of its particular significance in this communication, a fourth type must be added to those already outlined above, namely the microscopic fissures in the petrosa which are occasionally found associated with trauma to the skull. As a rule these fissures cannot be detected on gross examination, and, while they have at times been demonstrated roentgenologically, the diagnosis is almost invariably made by histological studies.

REPORT OF CASE

History.—A man (G. T.) aged 43 was admitted to the medical service of the Mount Sinai Hospital with signs of advanced lobar pneumonia, from which he died within two days. There was a history of skull fracture which had been sustained eight years previously when the patient, while working as a longshoreman, fell from a height of about 30 feet. He lost consciousness at the time and passed into a state of coma. There was bleeding from the left ear. On regaining consciousness he began to experience deafness and tinnitus in the left ear. This was followed by attacks of vertigo which prevented him later from carrying on his work, paralysis of the left side of the face and left arm and inability to masticate food because of pain on the left side of

From the Otolaryngological Service of Dr. R. Kramer and the Department of Laboratories of the Mount Sinai Hospital.

1. Grove, W. E.: Skull Fractures Involving the Ear: A Clinical Study of 211 Cases, Laryngoscope **49**:678 and 833, 1939.

2. Voss, O.: Die Chirurgie der Schädelbasisfrakturen auf Grund 25 jähriger Erfahrungen, Leipzig, Johann Ambrosius Barth, 1936.

the mouth. He also experienced pain in the left ear, severe left-sided headaches, poor vision in the left eye and diplopia. These symptoms had continued up to the time of his fatal illness.

Examination.—Because of the patient's poor physical condition, a complete otological and neurological examination, including hearing and vestibular tests, could not be carried out. Examination by the medical house staff, however, disclosed no abnormalities in the external and middle ears. Ocular movements and the fundi oculi were normal.

Necropsy Findings.—Evidence of extensive lobar pneumonia was found. The skull and calvaria were normal; the dura was slightly adherent to the skull in the region of the left petrosquamous fissure in which place the bone was somewhat roughened and nodular, but there

Fig. 1.—The minute fracture line at *F* running from the fallopian canal to the external semicircular canal is shown. The labyrinthine spaces are almost entirely occupied by new bone. Fibrous tissue bands can be seen bridging across the antrum. *A* represents the antrum, *ESC* the external semicanal, *FN* the facial nerve and *PSC* the posterior semicanal.

was no gross evidence of fracture of the vault or of the petrous pyramids. Histological sectioning of the brain disclosed a chronic productive leptomeningitis and toxic encephalitis.

Histological Observations of the Left Temporal Bone.—The periantral spaces, particularly those adjacent to the cortex, were lined by a thickened mucous membrane. The antrum itself was bridged over by bands of dense fibrous connective tissue (fig. 1), some of which formed the walls of cystic cavities. The picture presented was one seen in the late stages of a chronic adhesive inflammatory process. There were minute fractures of the tegmen tympani, and within the epitympanum could be seen small fragments of displaced bone, probably parts of intercellular septums bound down by dense scar tissue. The head of the malleus was ankylosed to the roof of the tympanum (fig. 2). The incus was dislocated downward (fig. 3) and was detached

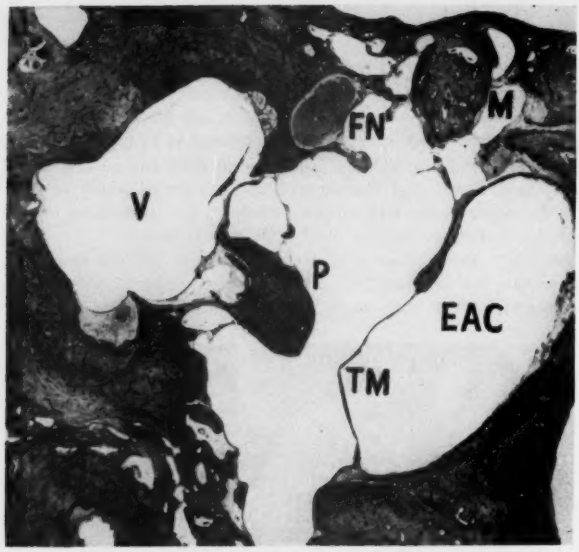

Fig. 2.—Section through the attic region showing ankylosis of the head of the malleus. The thickening and scarring of the upper part of the tympanic membrane are also demonstrable. *EAC* represents the external auditory canal, *FN* the facial nerve, *M* the malleus, *P* the promontory, *TM* the tympanic membrane and *V* the vestibule.

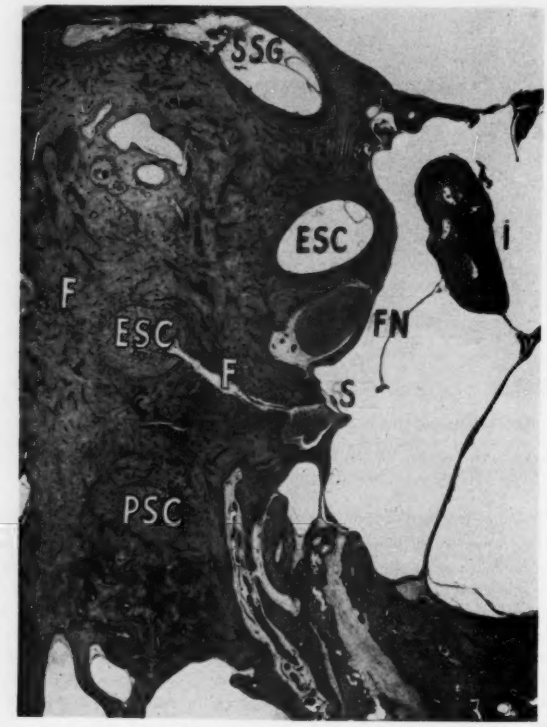

Fig. 3.—The relatively open peripheral portion of the fracture line extending from the canal for the stapedius muscle to the external semicanal can be seen. Complete bony union has taken place in the more central portion of the fracture line. *ESC* represents the external semicanal, *F* the line of fracture, *FN* the facial nerve, *I* the incus, *PSC* the posterior semicanal, *S* the stapedius muscle and *SSC* the superior semicanal.

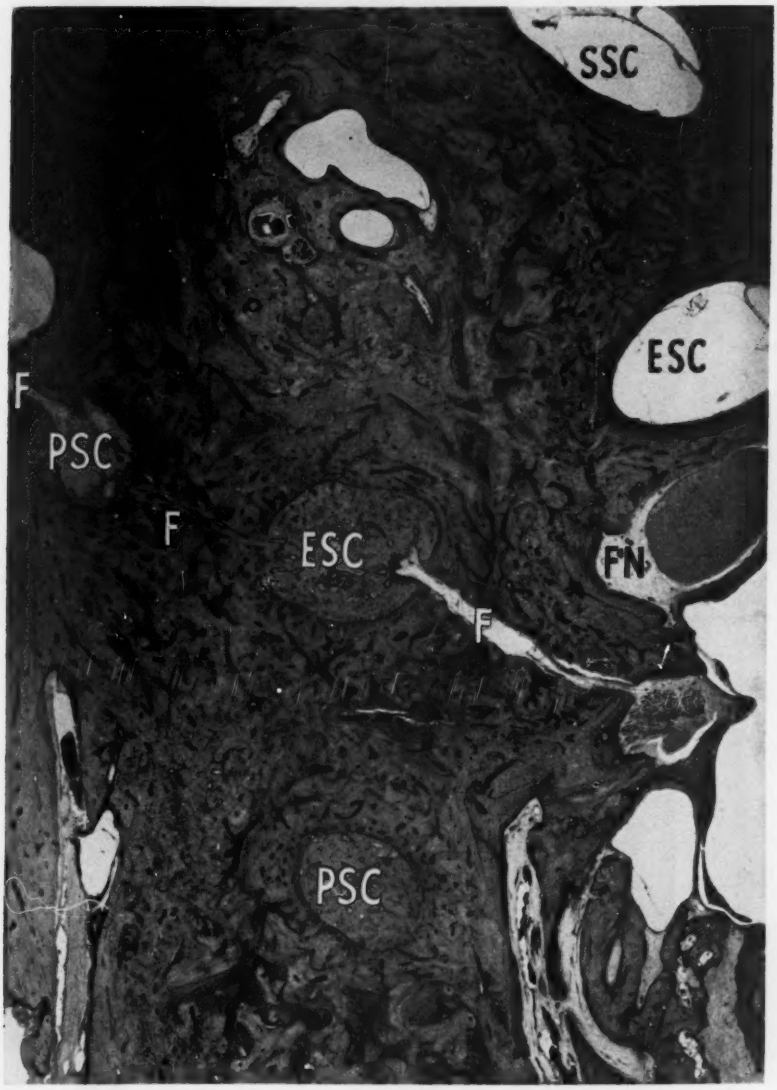

Fig. 4.—Higher magnification and a larger field than those of figure 3. The fracture can here be followed posteriorly to the dura. Note that healing by bone has taken place only in the central portion of the fracture, while at both peripheral portions the fragments are still united by connective tissue. *ESC* represents the external semicanal, *F* the line of fracture, *FN* the facial nerve, *PSC* the posterior semicanal and *SSC* the superior semicanal.

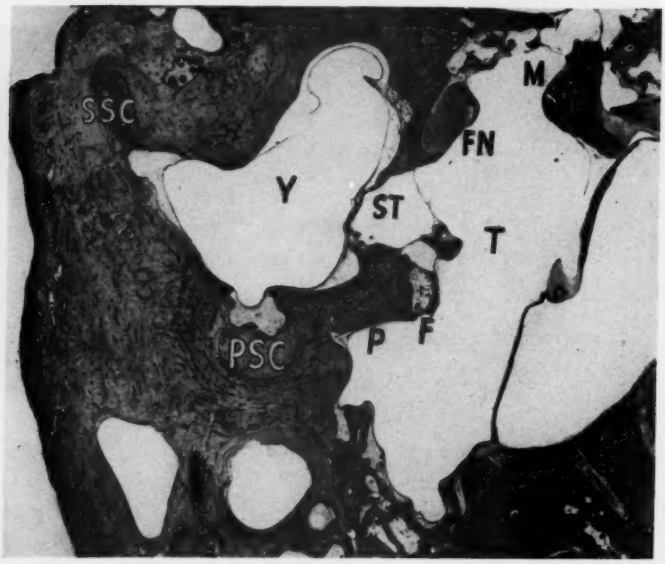

Fig. 5.—The fracture line through the promontory is shown, the bony fragments being united by only connective tissue. *F* represents the fracture, *FN* the facial nerve, *M* the malleus, *P* the promontory, *PSC* the posterior semicanal, *SSC* the superior semicanal, *St* the stapes and *T* the tympanum.

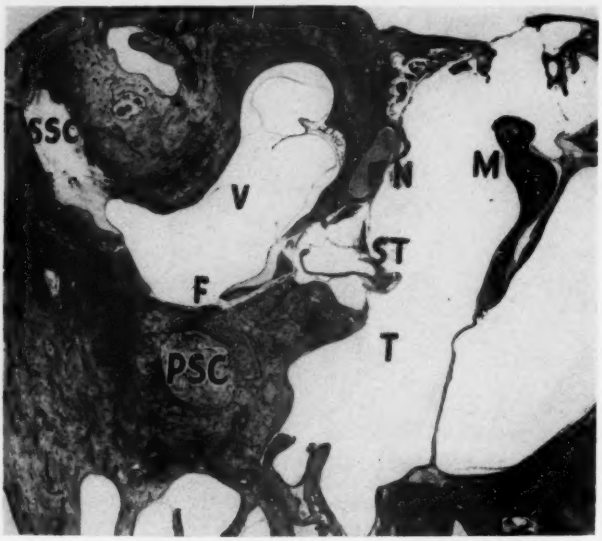

Fig. 6.—The fracture in the region of the oval window establishes a communication between the tympanic cavity and vestibule. There is no bony union, healing having taken place by only connective tissue. *F* represents the fracture, *FN* the facial nerve, *M* the malleus, *PSC* the posterior semicanal, *St* the stapes, *SSC* the superior semicanal, *T* the tympanic cavity and *V* the vestibule.

from both the malleus and the stapes. The stapes was partially luxated from the oval window. The tympanic membrane was intact but was scarred and thickened, apparently due to previous curling up on itself of the connective tissue layer in the process of repair (fig. 2). Small frac-

Fig. 7.—Higher magnification of fig. 6 showing fracture line *F* in greater detail. Note small blood vessels at tympanic opening of the fracture.

tures were seen in the posterior and anterior bony canal walls. They were lined by connective tissue, but the skin covering the external canal was entirely intact.

Minute fissures coursing transversely through the labyrinthine capsule could also be clearly demonstrated (figs. 3 and 4). They appeared to branch off in many directions involving the semicircular canals, the promontory (figs. 5 and 8) and the vestibule (figs. 6 and 7). One of

Fig. 8.—Fracture (*F*) through the promontory with relatively wide displacement of the lower fragment. There is little evidence of bony union at this site.

these fracture lines could be traced from the middle ear cavity across the labyrinthine capsule to the posterior fossa (fig. 4); others were found to involve the fallopian canal (fig. 1) and the canal for the stapedius muscle (figs. 3 and 4).

The fracture lines through the petrosa seemed to have healed only partially by bony callus, while at many sites the fragments were still united by a dense or even by a loose connective tissue (figs. 4, 7 and 8). This faulty and incomplete union of the fragments was particularly

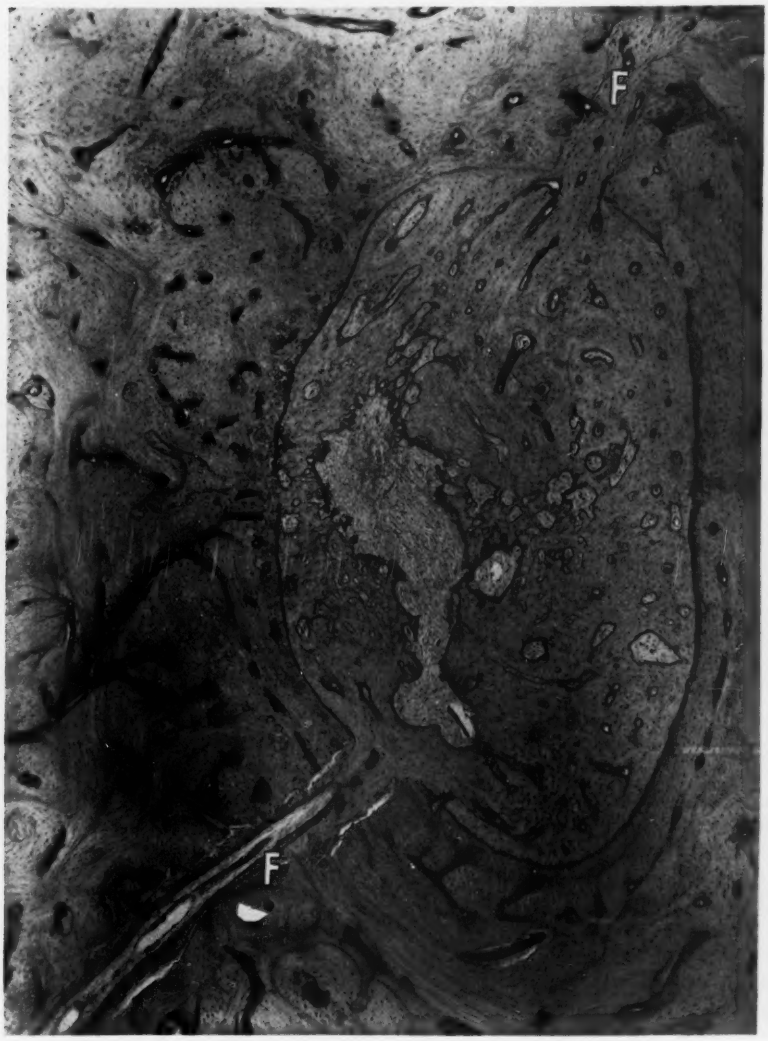

Fig. 9.—The new bone within the labyrinth appears to have proliferated into the line of fracture (*F*) at opposite ends of the canal.

noticeable in the vicinity of the middle ear cavity and vestibule. The microscopic fissure in the promontory, for example, was occupied almost only by fibrous tissue (fig. 8). Toward the center of the petrosa and near the posterior fossa, however, bony union was more complete.

In the region of the fracture line the labyrinthine spaces were almost entirely replaced by newly formed bone (figs. 1, 3, 4 and 9), the endolymphatic as well as the perilymphatic space being involved. This new bone can be traced within the labyrinth for a considerable distance beyond the site of fracture, where it appeared to be in the process of replacing the previously formed connective tissue (fig. 6). From there on the inflammatory changes within the labyrinth became gradually less pronounced until normal-appearing labyrinthine structures could be detected. The new bone formation was most prevalent at the margins of the labyrinthine spaces; it seemed to start from the endosteal lining and gradually fill in the entire lumen by a process of budding of osteoid tissue. The osteogenesis within the labyrinth appeared to be in an active state even at this late stage. The newly formed bone could be readily delineated from the adjacent bony capsule despite the rich vascular intercommunication of capillaries. The new bone within the labyrinth seemed to have proliferated for a distance into the adjacent fracture line and apparently had contributed to some degree toward the healing of the fracture by bony union (fig. 9).

Atrophic degenerative changes had taken place in the sensory nerve endings of the cochlea, in the ganglion cells of the spinal ganglion (which were diminished in number and partially replaced by fibrous tissue) and in the nerve fibers within the lamina ossea spiralis. These changes were particularly noticeable in the first turn of the cochlea. The nerve endings in the superior and external semicircular canals, on the other hand, were fairly well preserved. The cochlear canal was markedly dilated (hydrops) in the first and second turns, Reissner's membrane being bound down by scar tissue to the modiolus. Degenerative changes were also observed in both branches of the acoustic nerve and in the facial nerve within the internal auditory meatus. The pia-arachnoid surrounding the nerves was markedly thickened and chronically inflamed. The periosteum lining the internal auditory meatus and fallopian canal was also appreciably thickened, as was the dura in the region of the geniculate ganglion to which it was intimately adherent.

COMMENT

This case is of particular significance because it afforded a rare opportunity to study histologically the late changes which have occurred after fracture of the petrosa caused by head trauma. Though the early changes associated with fractures have been studied rather extensively in humans [3] and experimentally in animals,[4] relatively few cases are on record in which histological observation of the late changes have been made.

The patient sustained combined longitudinal and transverse fractures of the temporal bone eight years before he died, death being due to an unrelated cause. It is unfortunate that all the pertinent clinical findings at the time of the injury and in the years that followed could not be ascertained. Nevertheless, sufficient data were obtained from the history to warrant making the diagnosis of fracture of the petrosa and localizing the site of fracture with a degree of certainty. It was known, for example, that the patient lost consciousness immediately after the injury, that there was bleeding from the left ear and that a left facial paralysis, pronounced deafness and vertigo developed.

On postmortem examination there was no definite gross evidence of fracture of the skull or of the petrosa. It was only on histological examination that the microscopic fissures or minute fractures coursing through the petrosa and involving the labyrinthine capsule were disclosed, together with evidence of fracture through

3. (*a*) Passow, A.: Die Verletzungen des Gehörorganes, Weisbaden, J. F. Bergmann, 1905. (*b*) Stenger: Beitrag zur Kenntnis der nach Kopfverletzungen auftretenden Veränderungen im inneren Ohr, Arch. Ohrenh. **79**:43, 1909.

4. Footnote *3b*. Schönbauer, L., and Brunner, H.: Schädelbasisbrüche, in Alexander, G., and Marburg, O.: Handbuch der Neurologie des Ohres, Berlin, Urban & Schwarzenberg, 1928, vol. 2, p. 327.

the roof of the tympanum and through the external auditory canal. The microscopic fissures were observed chiefly in the region of the oval and round windows, and surprisingly enough, though eight years had elapsed since the injury, they had shown little tendency toward healing, only partial bony union having taken place, while to a great extent the fragments were united by fibrous tissue or by only very loose connective tissue.

That microscopic fissures of the petrosa can occur with injuries to the skull has been known for many years. Their pathological features have been studied by Nager,[5] Ulrich,[6] Voss[2] and others. Manasse[7] in 1907 reported an interesting case in which he described histologically these fissures in a patient who had died 15 years after skull trauma. The pathological findings were in many respects similar to those observed in the case herein reported.

That microscopic as well as gross fractures of the petrosa heal differently from fractures of other parts of the body has also been known for many years, the essential difference being that in petrosal fractures closure by bony union is either incomplete or fails entirely, while in fractures elsewhere complete bony union is the rule. Furthermore it has been shown by microscopic studies that in petrosal fractures osteogenesis does not take place to the same degree throughout the entire extent of the fracture. Whereas bony union usually takes place at the periphery of the petrosa near the cortex, closure by only connective tissue takes place in the central portion, i. e., in the region of the inner tympanic wall. This difference in the character of healing can be attributed to the rather unique sluggish response to trauma exhibited by the endochondral layer of the bony labyrinthine capsule. In this connection it is of interest to note that in the experiments recently performed on monkeys in an effort to determine the causes for closure of the fistula after fenestrating the bony labyrinthine capsule, Holmgren,[8] Engström,[9] Fowler Jr.,[10] Lindsay,[11] Shambaugh Jr.[12] and Lempert, Meltzer, Schall and Wolff[13] have observed that though none of the three layers of the capsule is immune to osteogenesis, the endochondral layer appears to react less readily to trauma than does the endosteal or periosteal layer.

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5. Nager, F. R.: Über Spätmeningitis nach Labyrinthfraktur, Acta oto-laryng. **14**:127, 1930.

6. Ulrich, K.: Verletzungen des Gehörorgans bei Schädelbasisfrakturen, Acta oto-laryng. (supp.) **6**:1, 1926.

7. Manasse, P.: Zur pathologischen Anatomie der traumatischen Taubheit, Arch. path. Anat. **189**:188, 1907.

8. Holmgren, G.: Surgical Therapy in Otosclerosis, in Nelson Loose-Leaf Surgery of the Ear, New York, Thomas Nelson & Sons, 1938, chap. 17.

9. Engström, H.: Über das Vorkommen der Otosklerose nebst experimentellen Studien über chirurgische Behandlung der Krankheit, Acta oto-laryng. 1940, supp. 43, p. 1.

10. Fowler, E. P., Jr.: Critique of Surgical Treatments for Deafness, Canad. M. A. J. **43**:546 (Dec.) 1940.

11. Lindsay, J. R.: Histologic Observations on the Healing of Labyrinthine Fistulas in Monkeys, Arch. Otolaryng. **43**:37 (Jan.) 1946.

12. Shambaugh, G., Jr.: The Fenestration Operation for Otosclerosis, J. A. M. A. **130**:999 (Aug. 13) 1946.

13. Lempert, J.; Meltzer, P.; Schall, L., and Wolff, D.: Osteogenesis Following Fenestration of Vestibular Labyrinth of Rhesus Monkey, Arch. Otolaryng. **46**:512 (Oct.) 1947.

Failure of the fracture line to close over entirely by bony callus was always considered important from the clinical standpoint because it remained a constant potential pathway for the spread of infection from the middle ear to the labyrinth. Cases have been reported in which meningitis resulted from a relatively mild infection of the middle ear occurring at any time from a few days to many years after the injury.[14] It is therefore readily understandable why the prognosis in fractures of the temporal bone was necessarily guarded. This held true for fractures of the temporal bone in general and applied particularly to transverse fractures of the petrosa involving the labyrinth. With the advent of antibiotics, however, the hazard of intracranial complications has been greatly diminished. These fractures need no longer be considered so serious a problem as in the past. It is of interest that in the case reported which antedated the antibiotics, the chances for bacterial invasion of the intracranial contents were particularly good, since there was a combined longitudinal and transverse fracture with hemorrhage from the ear and with open communications between the middle ear and both the labyrinth and the meninges. In spite of this, an intracranial complication did not supervene.

The hemorrhage from the middle ear, observed clinically, was by itself fairly conclusive evidence of a longitudinal fracture of the petrosa, but the diagnosis was only definitely established subsequently by the histological changes of ankylosis of the head of the malleus with displaced fragments of intercellular bony septums and by the observation of scarring of the tympanic membrane.

The pronounced bony infiltration of the labyrinthine spaces in the region of the fracture was also of interest. It undoubtedly represented the final stages in the process of organization and fibrosis of the hemorrhage that had taken place within the labyrinth at the time of injury. Because the osteogenesis in these cases seemed to be initiated by the endosteal lining and to progress to a degree in which the labyrinthine spaces were almost entirely occluded, Manasse termed this condition "periostitis obliterans." The histological picture is quite similar to that seen in the late stages of labyrinthitis due to causes other than fracture, e. g., epidemic meningitis, etc. It should be stated in passing that while hemorrhage into the labyrinth can occur as a result of trauma to the skull, with or without fracture, it is observed oftenest in transverse fractures of the petrosa.

Paralysis of the facial nerve is a frequent complication of skull fracture. It occurred in 29 of the 211 cases reported by Grove,[1] or in 14 per cent, and in 18 per cent of the longitudinal and in 31.5 per cent of the transverse fractures. The paralysis is usually due to tearing or stretching of the nerve fibers anywhere in its course through the fallopian canal or to hemorrhage within the nerve proper. While the function of the nerve is known to return completely or to improve in the majority of cases, it may be lost permanently in some. An important factor that must be considered is the time of onset of paralysis following injury; as a general rule, paralysis occurring immediately after trauma gives a poor prognosis and if it persists may offer good grounds for surgical treatment. Kettel [15] in a recent publication outlined the criteria on which he bases his indications for operation on the facial nerve. In the case herein presented the facial paralysis occurred immediately

14. Footnote 5. Fraser, J. S., in discussion on Nager.[5]

15. Kettel, K.: Peripheral Facial Paralysis in Fractures of the Temporal Bone, Arch. Otolaryng. **51**:25 (Jan.) 1950.

after trauma and persisted thereafter without any evidence of return of function. The exact site of injury to the nerve could not be definitely determined by histological study, but the weight of evidence favored the region of the geniculate ganglion.

The vertigo and deafness experienced by the patient can be readily correlated with the pathological findings, namely the extensive reactive inflammatory changes within the semicircular canals, the vestibule and the cochlea and the secondary atrophic degenerative changes within the cochlear and the vestibular nerves and their end organs.

The patient's difficulty in masticating food on the left side of the mouth can best by explained by the minute fractures in the external auditory canal communicating with the glenoid fossa and by the injury to the facial nerve with loss of function of the muscles on that side.

SUMMARY

The main forms of fracture of the petrous pyramid are outlined and their characteristic features described.

The clinical and histopathological findings in a case of combined longitudinal and transverse (microscopic) fractures of the temporal bone in a patient who died eight years after injury to the skull are recorded and correlated. Of the histological changes noted, perhaps one of the most striking was the relatively incomplete healing that took place within the fracture lines of the petrosa in spite of the chronicity of the condition.

Microscopic fractures of the petrosa in general are discussed. Their histological features, their rather unusual reparative process and their clinical significance in the transmission of infection from the middle ear to the labyrinth and intercranium are stressed.

ORBITOETHMOIDAL OSTEOMA

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ORBITOETHMOIDAL osteoma is not common. Excellent reports on osteoma of the paranasal sinuses have been made by many investigators. For a brief review of the literature, the reader is referred to the paper by Vadala and Somers.[1] Novick's [2] concise and well illustrated article covers such phases as etiology, embryology and histology. Sprowl's [3] case of orbitoethmoidal osteoma was very similar to the case we report.

REPORT OF A CASE

A man aged 23 reported to the Eye, Ear, Nose and Throat Clinic Jan. 27, 1949, complaining of aching, burning and swelling in the left eye of one day's duration. He stated that he had had previous similar episodes but that this one was the severest. He appeared somewhat dull mentally, and any more than a vague history was impossible to obtain.

On examination the left eyelids were seen to be moderately inflamed but soft. The conjunctiva was edematous and bulged over the lid margin temporally. The pupil was round and reacted normally to light. The media and fundus were normal. The globe was proptosed about 1 cm. There was limitation of motion in all planes. It is interesting to note that the patient had not complained of diplopia until it was called to his attention. Vision was 20/20 and he read Jaeger type 1 with each eye. The results of the physical examination were otherwise normal.

A roentgenogram revealed a large, irregular mass measuring 2 by 2.5 cm. in diameter in the left ethmoid labyrinth area and extending into the medial posterior portion of the orbit. The mass was reported as being of hard bony density.

After admission to the hospital the patient's chief complaint was headache. He was given penicillin therapy and bed rest. Chemosis subsided within 36 hours. On February 1, the tumor was removed in one piece through a curved incision in the eyebrow extending down to the side of the nasal bridge. The tumor appeared to involve most of the ethmoid labyrinth and was attached by a separate pedicle to the superior wall of the orbit. In detaching this pedicle the dura was exposed for an area about 6 mm. in diameter. There was no fusion with

1. Vadala, A. J., and Somers, K.: Osteoma of the Frontal Sinus, Arch. Otolaryng. **50**:618-633 (Nov.) 1949.

2. Novick, J. N.: Osteoma of the Frontal Sinuses, Arch. Otolaryng. **46**:655-669 (Nov.) 1947.

3. Sprowl, F. G.: Orbito-Ethmoidal Osteoma, Ann. Otol., Rhin. & Laryng. **45**:886-890 (Sept.) 1936.

the orbital contents; consequently trauma to these parts was minimal.[4] Postoperatively he was fairly comfortable. The drain was removed February 3; sutures were removed February 7, and the wound was left undressed February 11. At this time ocular swelling had subsided so that the associated parallel movements of the eyes could be checked. They appeared normal, and there was no diplopia. There was no proptosis. Edema of the upper eyelid gradually

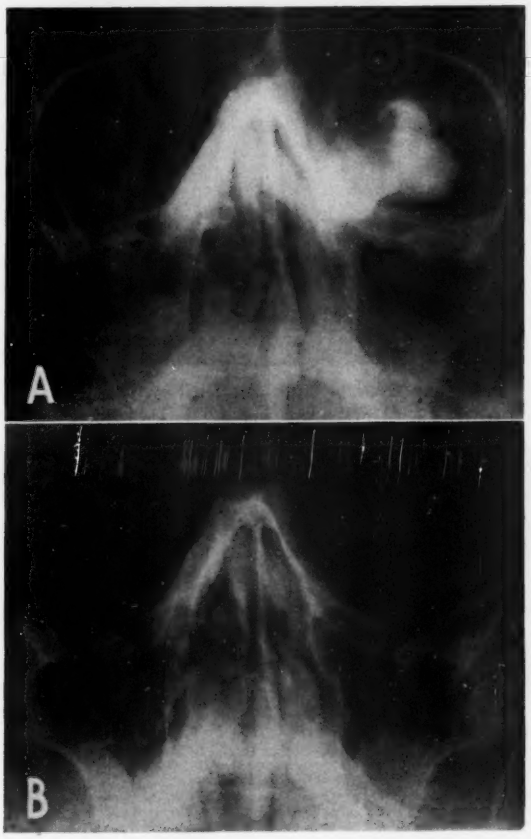

Fig. 1.—*A*, before surgery. Note the tumor extends into the ethmoid region. *B*, after surgery. Careful comparison of this roentgenogram with the upper one reveals the full extent of the tumor. Note polyp-like thickening of the mucosa of the left maxillary sinus and mild thickening of the mucosa of the right maxillary sinus.

subsided, and he became mentally alert. Recovery was complete, and he was discharged March 10.

4. The operation was performed by Dr. William C. Wolfe, Louisville, Ky., consultant in Otorhinolaryngology, Station Hospital, Fort Knox, Ky.

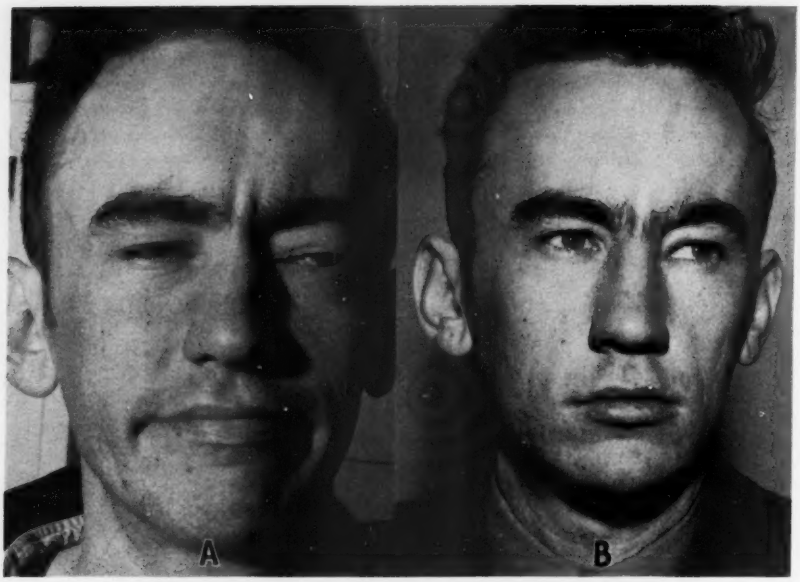

Fig. 2.—*A*, before surgery. Note proptosis of the left eye. *B*, after surgery. There was complete recovery. Compare this figure with *A* to observe the full extent of the proptosis.

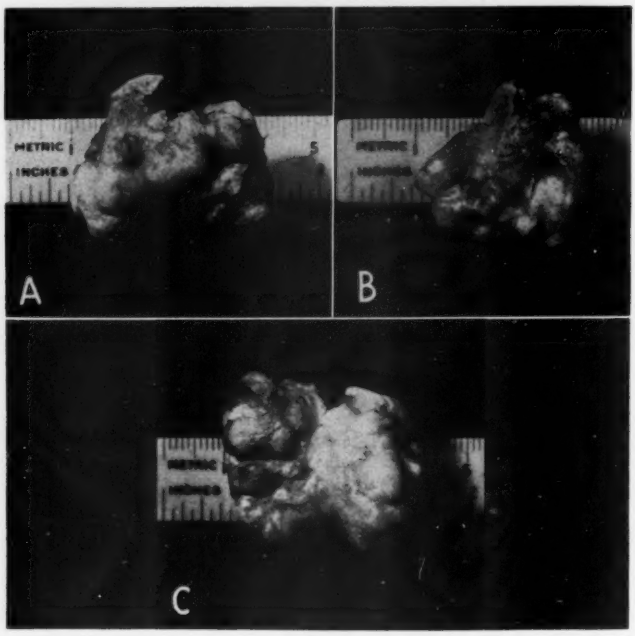

Fig. 3.—*A*, posterior surface of orbitoethmoidal osteoma. The projection upward is topped by the dural plate. The portion to the right (about one third of the tumor) is the ethmoidal portion. *B*, medial surface. The posterior surface is to the left. *C*, inferior surface. The ethmoidal portion is to the left.

The gross pathology report stated that the specimen consisted of a mass of firm calcified tissue, irregular in outline, measuring approximately 3.0 by 3.0 by 2.5 cm. The weight was 12 Gm. Displacement was 7 cc.

The histology report stated that the decalcified sections were made up of cancellous type bone supported by a delicate network of fibrous connective tissue. The superficial portions were made up of more compact osseous tissue. The bony spicules showed a lining of osteoblasts, and these in turn were adjacent to connective tissue. There was no evidence of malignant degeneration.

The diagnosis was fibro-osteoma.

MIXED TUMOR OF SKIN OF EXTERNAL AUDITORY CANAL

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AND
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THE PRESENCE of mixed tumors which look like those of the salivary glands in other than the usual sites is not common. Hence, the finding of such a neoplasm in the external auditory canal, a location in which none have hitherto been described, seems worth reporting.

REPORT OF A CASE

Clinical History.—A 37 year old Negro woman consulted one of us (M. R.) and described a small painless lump in the anteroinferior wall of the left external auditory meatus. She stated that it had been present for at least 10 years. Although it had grown slowly, there had been no noticeable increase in size for several years. The firm circumscribed nodule lay beneath the skin, which was freely movable. A preoperative diagnosis of chondroma was made and the mass excised without difficulty.

Surgical Specimen.—The excised specimen measured 2.5 by 1.3 by 1.7 cm. and was conical and firm. The overlying, slightly atrophic skin was freely movable. On section the cut surface was homogeneously white and of a cartilaginous consistency. At one pole, a small cyst containing clear, colorless glairy fluid was encountered.

Microscopically, deep in and toward the corium there was seen a variably broad zone of masses (figs. 1 and 2, *a*) of small oval to spindle cells in columns and sheets. They resembled the cells of the epidermal basal layer and were not unlike those of the sweat glands. Occasionally the cells were larger and had vesicular nuclei. Nuclear atypism and variation in cellular size and shape were absent. In many places the cells formed acinar structures which contained mucoid material; many acini were cystic (figs. 1 and 2, *b*). The lining cells were generally single layered but in some places were multilayered. In the latter areas, intercellular bridges were identified. There were rarely intraluminal papillary intrusions. Some cells had intracellular vacuoles and consequently resembled sebaceous glands because of the foamy cytoplasm. Occasionally, nests of epithelial cells manifested degeneration of their central portions so that the cells were separated although still connected by long intercellular processes. In one nest, for example, a sebaceous gland was observed at one end, while at the other degeneration of the central portion was exhibited.

Deep to this epithelial zone was the core (figs. 1 and 2, *c*) of the specimen. It was composed of many branching cells embedded in a matrix of homogeneous mucoid substance penetrated by thin collagenous fibrils and thus formed a loose lacework running in all directions. The cells were usually triangular or round, with scanty acidophilic cytoplasm. Often there were delicate processes arising from the cytoplasm which extended into the interstitial tissues. Vacuolization of the latter was frequently encountered. More deeply, the stromal matrix was hyalinized and took on a cartilage-like appearance. In many areas there was a gradual transition from the cartilaginous zones to the myxoid connective tissue, and necrosis and cyst formation were frequently encountered.

COMMENT

This case presents many features common to mixed tumors of the parotid gland. It occurred in the age group in which these new growths are most prevalent,

From the Department of Pathology, St. Joseph Hospital, Fort Wayne, Ind.

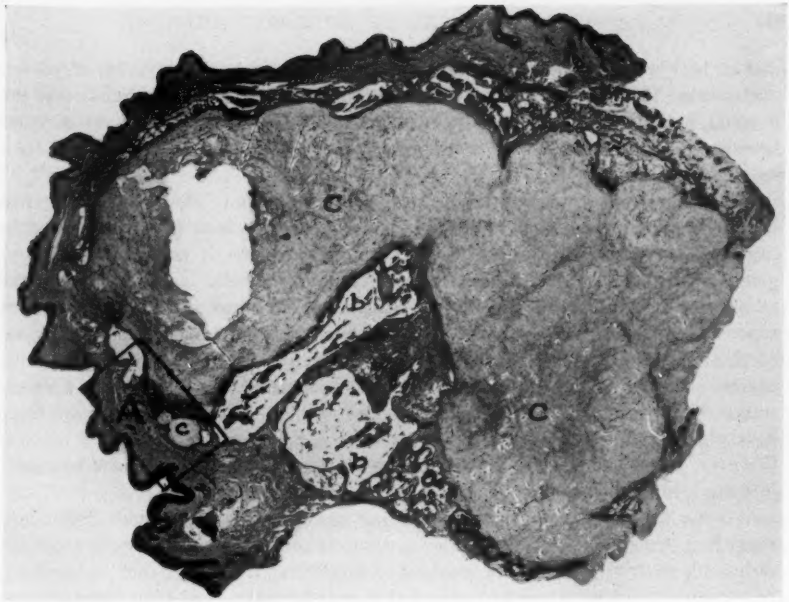

Fig. 1.—Section of major portion of the mixed tumor of the external auditory canal showing (*a*) the laver of epithelial structures resembling skin appendages with (*b*) acini and cystic dilatation and (*c*) a core of cartilage-like tissue. Hematoxylin and eosin; × 11.

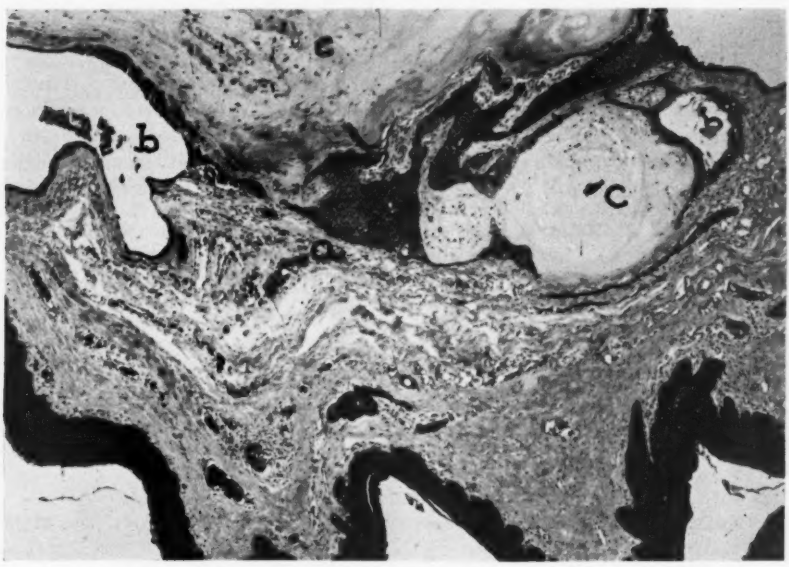

Fig. 2.—A portion (*A* in fig. 1) of mixed tumor of the external auditory canal showing (*a*) the epithelium with glandlike formation, (*b*) the cystic formation and (*c*) the cartilage-like core. Hematoxylin and eosin; × 70.

that is, between 20 and 40,[1] although the occurrence of growths in children [2] is not uncommon. The swelling was present for at least 10 years prior to admission to the hospital, and Benedict and Meigs [3] found in their series an average of seven years between the time the patient first noticed the swelling and his admission to a hospital.

The diagnosis of mixed tumor in this case was not difficult. The interest lies in the presence of sebaceous glands. Although there have been very few published cases of mixed tumors of the parotid gland which contained sebaceous glands,[4] development of sebaceous glands from intralobular ducts of the normal lobule of a parotid gland which showed recurrence of typical mixed tumor has been reported.[5] It is also interesting to note that sebaceous glands develop in the region of the deep aspect of the cheek during puberty, the site of development of the parotid gland from the ectoderm. In Morehead's publication [6] reporting a mixed tumor of the skin of the left breast, there was a brief description of the epithelial cells differentiating into structures resembling sebaceous glands. In our patient, however, there was transition of the sebaceous gland into epithelial neoplasm and, in turn, into the cystic and acinar structures.

Anomalies of sebaceous glands are not uncommon. Twort and Bottomley [7] suggested that the fatty acid breakdown products of sebaceous secretions, especially oleic acid, render the cells more sensitive to stimulating influences, such as hormones or chronic irritation. Simard [8] believed that mixed tumors have their origin locally, that is, from sweat glands, rather than from displaced embryonic tissues through the various selective differentiations of the epithelium and then modifications of stroma into cartilaginous tissue and the like by metaplasia. It appeared to him that the modifications and metaplasia appeared to have an association with the mucous secretion of the epithelial neoplastic tissues.

It has been proposed that "transformation from epithelium to cartilage might be favored by necrosis, hemorrhage, edema and inflammation subsequent to trauma, stress and strain leading to a dispersal of the cells with the formation of a mucinous and cartilaginous matrix." [9] That such may occur is illustrated by Eggers' report [10] of a mixed tumor of the upper lip in which there was antecedent trauma. Another similar tumor [11] appeared after a severe blow 12 years before excision. Hirsch's [12]

1. Brown, J. B.; McDowell, F., and Fryer, M. P.: Surg., Gynec. & Obst. **90**:257, 1950.
2. Rawson, A. J.; Keep, C. E.; Horn, R. C., and Royster, H. P.: Surg., Gynec. & Obst. **90**:307, 1950.
3. Benedict, E. B., and Meigs, J. V.: Surg., Gynec. & Obst. **51**:337, 1930.
4. Harvey, W. F.; Dawson, E. K., and Innes, J. R. M.: Debatable Tumours in Human and Animal Pathology, London, Oliver & Boyd, Ltd., 1940, p. 24.
5. Hartz, P. H.: Development of Sebaceous Glands from Intralobular Ducts of Parotid Gland, Arch. Path. **41**:651 (June) 1946.
6. Morehead, R. P.: Mixed Tumors of Skin: Report of Cases, with Consideration of Histogenesis of Mixed Tumors of Organs Derived from Ectoderm, Arch. Path. **40**:107 (Aug.) 1945.
7. Twort, C. C., and Bottomley, A. C.: Lancet **2**:776, 1932.
8. Simard, L. C.: Am. J. Cancer **33**:182, 1938.
9. Highman, B.: Mixed Tumor of Salivary Gland Type on Left Hand, Arch. Path. **37**:387 (June) 1944.
10. Eggers, H. E.: Mixed Tumors of Lip, Arch. Path. **26**:348 (July) 1938.
11. Pilcher, R.: Brit. M. J. **1**:967, 1937.
12. Hirsch, E. F.: Subcutaneous "Mixed" Tumor (Salivary Gland Type) of Left Thigh, Arch. Path. **16**:494 (Oct.) 1933.

report of a tumor of the thigh, which was subjected to repeated injury, may be included. Thus, it is not unlikely that trauma may be a predisposing factor. Certainly a tumor in the ear canal is not free from repeated physical irritation.

Li and Yang [13] classified mixed tumors in two groups, intraoral and extraoral. In the first group they included the neoplasms originating from oral ectoderm and lying within the oral cavity, such as those of palate, gum, tongue and salivary glands. In these instances the embryonal rests were considered as causing the formations, together with the salivary and oral glands, from invagination of the oral ectoderm. In the second group they placed the new growths originating extraorally: (1) tumors derived from ectodermal inclusions produced by fusion of branchial clefts and other fissures of the head and neck; (2) neoplasms of the nasal cavity and its accessory sinuses arising from rests formed along with normal mucous glands of these regions; (3) tumors of the orbits derived from rest formed from the conjunctiva together with anlages of lacrimal glands, and (4) other mixed tumors of lips, face, eyebrow, scalp, etc., assumed to have arisen from rests from the integument formed with the anlages of the hair follicles.

The majority of extrasalivary gland mixed tumors have been reported as situated in the head close to branchial and other embryonic fissures. These include the skin of nose and ear, as well as the breast and sternum.[6] Other sites include lips,[10] palate,[14] lacrimal glands [15] and the skin of the thigh,[12] of the scalp,[16] of the palm [8] and of the ear pinna,[13] the latter being the only one hitherto described on the ear.

SUMMARY

A mixed tumor had been present for at least 10 years in the skin of the auditory canal of a 29 year old Negro woman. Abnormal development of sebaceous glands, perhaps with the accelerating factor of repeated trauma, was held responsible for its formation. The ear has hitherto been reported only once as the site of a mixed tumor, and that once the tumor was on the pinna.

13. Li, P. L., and Yang, C.: Am. J. Cancer **25**:259, 1935.
14. D'Aunoy, R.: Am. J. Path. **6**:137, 1930.
15. Verhoeff, F. A.: J. M. Res. **13**:319, 1904-1905.
16. Delaney, P. A.: Mixed Tumor of the Scalp, Arch. Path. **12**:145 (July) 1931.

Progress in Otolaryngology

ALLERGY

Summaries of the Bibliographic Material Available in the Field of Otolaryngology for 1949

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AND
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OMAHA

THE LITERATURE on allergy has continued to accumulate rapidly during 1949. Much has been written on the treatment of various conditions particularly by the antihistamine drugs. Of the antihistaminics the older ones, namely diphenhydramine (benadryl®) and tripelennamine (pyribenzamine®) have received less attention than formerly, but their place has been taken in the literature by a rapidly growing list of newer ones. A new drug, pituitary adrencorticotropic hormone (ACTH), has shown promise in the treatment of allergic conditions. Its place is only beginning to be established, but a few interesting papers on this material have appeared during the past year.

NOSE AND THROAT

In a discussion of respiratory allergies Wittich [1] points out the extreme frequency with which these conditions occur. He discusses the clinical observations in nasal allergy, including the pallor and bogginess of the mucosa, the tendency toward edema and polyposis and the cytology of nasal smears. In smears 10 per cent of the eosinophils occurring in clumps is considered indicative of allergy. The problems encountered in roentgenography of the sinues are discussed and evaluated. Wittich feels that ideal treatment should consist of preventive measures, particularly the removal of as many offending allergens as possible. The importance of immunological measures is emphasized. Antihistamine drugs are to be regarded as palliative only, and it is pointed out that patients with nasal allergies may still develop asthma while under treatment with them. The greatest value of the antihistaminics is considered to be in conjunction with immunological procedures. Moderate doses given half an hour before injection will aid in reducing the incidence of general reactions and will make the administration of larger doses of allergens possible.

Craddock [2] has analyzed the findings in 80 patients with perennial nasal allergies who had had symptoms for from one year to as long as 30 years. Some of these patients had been under allergic management for 15 years. Sixteen had been under management for only one year. The symptoms complained of included nasal obstruction (48 cases), symptoms worse at night (33), sneezing (32), postnasal drip (32), fatigue (26), cough (24), headache (23), asthma (16), constant or recurring colds (12), itching eyes (12), joint pains (11), sinusitis (10), indiges-

1. Wittich, F. W.: Diagnosis and Treatment of Common Forms of Respiratory Allergy, Minnesota Med. **32**:702-709, 1949.

2. Craddock, W. H.: Perennial Nasal Allergy, Ann. Otol., Rhin. & Laryng. **58**:671-679, 1949.

tion (6), anosmia (5) and a few others. Clinical findings included essentially normal results of examination in 31 cases. Excessive mucus was found in 29, hypertrophy in 11, boggy membrane in 9 and pale membrane in 22. Eight patients had polypi, and five had polypoid degeneration of the middle turbinate. Eosinophils were found in nasal smears of 53 patients.

Craddock emphasizes the importance of the history in these cases and considers the general management of the patient very important. He feels that immunization therapy for inhalants and pollens is worth while. The elimination of etiological factors is important, and foods should be considered in establishing the etiology. Drugs should be used only when really needed and surgery avoided at least until allergic management has been instituted.

Maietta [3] has concluded that perennial allergic coryza is a disease entity and that the commonest causes are inhalants, ingestants and bacterial hapten sensitivity in 36 of the patients he studied and single or multiple inhalant and ingestant sensitivities in conjunction with bacterial hapten sensitivity in 143.

His outline of treatment includes desensitization and administration of penicillin aerosol intranasally (123,500 units with 3½ minims [0.21 ml.] of 1 per cent phenylephrine [neo-synephrine®] inhaled at each treatment). Vaccine therapy is mentioned, and the use of 1 per cent aqueous ephedrine solution as a decongestant followed by epinephrine solution U.S.P. and tyrothricin 1 : 5,000 is suggested. Surgery is recommended in cases of mucous polypi or edematous turbinates and to establish adequate drainage if other measures have not done so. Of the 180 cases, 149 are reported to have had excellent results on this regimen.

King [4] summarizes 150 cases of nasal allergy seen during a year in the Middle East. The group of seasonal cases is thought to be on a climatic rather than a pollen basis, as the region is one of sparse vegetation. Most of them occurred during the first and third quarters of the year, at which time the weather is the hottest. Associated symptoms included headache in 53 patients, deafness in 10, sore throat in 7, cough in 9 and asthma in 4. Nasal polypi were found in two cases. Sixty-one patients had sinus involvement.

Holmes, Goodall, Wolf and Wolff [5] discuss the etiology of nasal disorders. They feel that obstruction, swelling and hypersecretion are frequently incited by a virus but place particular emphasis on the part played by emotional factors. Nasal examinations of 112 patients indicated that nasal hyperfunction was commonly associated with situations productive of anxiety, hostility, conflict, guilt, frustration, etc. Over 4,000 observations were made on the above group of patients in conjunction with psychiatric studies. Microscopic examination of tissues obtained from some patients showed actual changes, such as edema, hypersecretion of the mucous glands and dilated blood vessels and lymphatics. It is concluded that the above changes are a part of a fundamental biological defense reaction.

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3. Maietta, A. L.: The Diagnosis and Treatment of Perennial Allergic Coryza, Ann. Allergy **7**:359-365, 1949.

4. King, P. F.: Some Manifestations of Nasal Allergy: A Survey of 150 Cases in the Middle East, J. Laryng. & Otol. **63**:501-510, 1949.

5. Holmes, T. H.; Goodall, H.; Wolf, S., and Wolff, H. G.: Evidence on the Genesis of Certain Common Nasal Disorders, Am. J. M. Sc. **218**:16-27, 1949.

The importance of an adequate history, and particularly a family history, in the diagnosis of allergic conditions is emphasized by Harrill.[6] He describes the characteristic appearance of the allergic nasal mucous membrane and recommends the search for eosinophils in nasal secretions. Harrill feels that in treatment sympatheticomimetic intranasal medication and surgery should be kept at a minimum.

According to Ashley,[7] a large proportion of nasal symptoms are allergic in origin. Nasal allergies can occur at all ages and may respond to only allergic management. Further emphasis is given to the importance of routine examination of nasal secretions for eosinophils. Dust is considered an especially important allergen, but molds, fungi, tobacco smoke and paper are also emphasized. In injection treatment Ashley recommends starting with small doses of very dilute antigen, which are built up only to the point at which relief is obtained. The time between injections should then be lengthened and treatment stopped when the patient is symptom free. If symptoms are aggravated during treatment, the dosage can be decreased.

Wallner[8] found that in 45 of 75 patients with definite nasal allergy there were mulberry enlargements on the inferior turbinate. He further found that in another group of 24 in which such enlargements were accidentally discovered, 12 could be shown to have nasal allergies. Studies of 15 of these mulberry growths which had been removed showed papillary hypertrophy of the epithelium and hyperplasia of the connective tissue stroma. A significant eosinophilic infiltration was the only difference found in growths of allergic and nonallergic origin. Mulberry growths are considered as irreversible and cannot be expected to disappear under allergic management. They should be removed if they cause obstruction.

An interesting study on nasal secretions is reported by Ingelstedt and Ivstam.[9] Fluorescein was injected intravenously, and the nasal secretions were examined for fluorescence. In acute infections and allergies fluorescence of the secretions was observed but not in chronic allergic rhinitis. It is concluded that actual exudation occurs in acute conditions, but that in chronic conditions there is only secretion from the glands.

Sinusitis has been discussed by a number of authors. Grove[10] believes that sinus disease is a very important cause of asthma. He is an advocate of surgical treatment for sinus disease in patients with asthma. Grove feels that in order to evaluate accurately the effect of sinus surgery on asthma it is necessary to determine whether or not the etiological factors include infection alone or infection associated with skin sensitivity. It is also necessary to consider the type of sinus operation performed. Immediate improvement after operation should not be expected but rather gradual improvement as the infection is eliminated.

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6. Harrill, J. A.: Recognition and Management of Allergic Conditions by Otorhinologists, North Carolina M. J. **10**:75-78, 1949.

7. Ashley, R. E.: Dust Therapy in Allergy of the Ear, Nose and Throat, Ann. Otol., Rhin. & Laryng. **58**:417-428, 1949.

8. Wallner, L. J.: Allergy as the Cause of Mulberry Hypertrophy of the Inferior Turbinate, Ann. Allergy **7**:258-265, 1949.

9. Ingelstedt, S., and Ivstam, B.: The Source of Nasal Secretion in Infectious, Allergic and Experimental Conditions, Acta oto-laryng. **37**:451-455, 1949.

10. Grove, R. C.: The Importance of Sinusitis in Allergic Manifestations, Laryngoscope **59**:653-665, 1949.

Schenck [11] is of the opinion that the ethmoid and maxillary sinuses are more prone to become involved in allergic reactions than the frontal or sphenoidal sinuses because of their close relation to the turbinates, which are considered as the primary shock organs. The turbinates in turn may become involved either by direct contact with inhalants or by contact with ingested allergens via the blood stream. The tendency toward early polyp formation in the ethmoid region is thought to be due to the thinness of the mucous membrane of the ethmoid cells. Polypi in this region may precipitate complications through pressure on adjacent structures. Nasal obstruction in turn, by necessitating mouth breathing, may permit allergens taken in to reach the lower respiratory tract more readily than in normal nasal breathing.

Glover [12] has listed some of the differential points between allergic and infectious sinus disease. Characteristics of allergy include a history of slow development, stuffy nose, fits of sneezing in the early morning, copious tenacious mucous discharge, hyperplastic mucosa and family history of allergy. He considers allergies to pollens, bacteria and various other allergens, with or without food sensitivities, the most important etiological factors in sinus disease. Allergic therapy should be instituted as soon as the responsible allergens are demonstrated.

In a study of over 200 cases of maxillary sinusitis, Ballantyne and Rowe [13] found eosinophils in numbers sufficient to establish a diagnosis of allergy in only a few. They suggest that allergic stimuli may impair ventilation in a certain small proportion of the whole group.

Wishart [14] has discussed the problem of pediatric rhinology and reviewed the literature on this subject for 1948. He feels that eosinophilia is nonspecific in character and points out a group of unrelated conditions in which it occurs.

Goodhill [15] is of the opinion that the commonest variety of sinusitis in children is allergic in origin and complicated by secondary infection. Such patients cannot be successfully treated without treating the allergy as well as the infection. Nose drops he considers of little value in sinusitis. Sulfonamides and antibiotics may be of value in acute sinusitis and may aid in the prevention of chronic involvement. Their topical application, however, is not recommended.

Green [16] recommends a method of administering pencillin in aerosol form to allergic patients with respiratory infections. His apparatus consists of an oxygen tank, a mask and a breathing bag. The method has been used in over 200 treatments on 79 allergic patients. It is said to be both convenient and effective. Prigal and Furman [17] have published preliminary observations on the use of bacitracin in aerosol form. They employed doses of from 12,000 to 134,000 units (usually 40,000 units) and feel that this form of therapy is indicated in cases in which the

11. Schenck, H. P.: Effects of Allergy on the Ethmoid Sinuses, Arch. Otolaryng. **49**:48-52 (Jan.) 1949.

12. Glover, C. H.: Management of Allergic Sinusitis, South. M. J. **42**:613-617, 1949.

13. Ballantyne, J. C., and Rowe, A. R.: Some Points in the Pathology, Diagnosis and Treatment of Chronic Maxillary Sinusitis, J. Laryng. & Otol. **63**:337-341, 1949.

14. Wishart, D. E. S.: Rhinology in Children: Résumé of and Comments on the Literature for 1948, Laryngoscope **59**:929-959, 1949.

15. Goodhill, V.: The Treatment of Sinusitis in Children, California Med. **70**:177-181, 1949.

16. Green, M. A.: Aerosol Penicillin in Allergic Patients with Respiratory Infections, Ann. Int. Med. **31**:260-270, 1949.

17. Prigal, S. J., and Furman, M. L.: The Use of Bacitracin, A New Antibiotic, in Aerosol Form: Preliminary Observations, Ann. Allergy **7**:662-675, 1949.

cultured organism is sensitive to bacitracin but not to penicillin or in patients with penicillin hypersensitivity.

Hynes [18] concludes that in allergic rhinitis administration of penicillin by aerosol is contraindicated except in proved cases of bacterial allergy or in patients with complicating sinusitis.

Local medication of the nasal cavities has been discussed on several occasions. Van Alyea and Donnelly [19] found no untoward effects of vasoconstrictors in a series of patients with various complicating conditions, including hypertension, thyroid disorders, diabetes and heart disease. Packard [20] reports on 250 cases of chronic rhinopharyngitis and allergic rhinitis treated with tyrothricin with benefit. Mill,[21] however, feels that many patients with allergic rhinitis aggravate that condition by the habitual use of vasoconstrictors, and Fabricant [22] discusses the ill effects of continuous administration of nose drops and antibiotics. He feels that secondary congestion can follow the use of vasoconstrictors and that there may be cases in which more congestion is due to this cause than to the underlying allergy. Brem and Zonis [23] have used buffered tripelennamine (2 per cent solution in the earlier cases, later a 0.5 per cent solution) applied topically on 81 patients with allergic rhinitis and report satisfactory to excellent results in 90 per cent of them. They point out, however, that such measures are temporary and that an antiallergic program is also necessary.

Saylor [24] has reported on the treatment of 99 cases of allergic and vasomotor rhinitis with hesperidin chalcone sodium in divided doses of 100 to 600 mg. daily. He obtained complete relief in 35 per cent of the patients, partial relief in 34 per cent and no relief in 25 per cent. Five per cent had side reactions including nausea, urticaria and aggravation of bronchial asthma. Saylor feels that the value of this treatment lies in the inhibition of an amine oxidase and thus an inhibition in the oxidation of epinephrine, which is in turn a natural antagonist to histamine. Baird [25] recommends the use of a sensitized mixed vaccine subcutaneously in the treatment of sinusitis. He has used this method successfully over more than 20 years.

The problem of tonsillectomy in allergic children is discussed by Clein [26] and Feingold.[27] Clein reports that in 136 children with recognized allergies which were adequately treated, regrowth of tonsils and adenoids after removal occurred in only 3 per cent. In a group of 60 others, 10 of whom were suspected of being allergic,

18. Hynes, F. J.: Penicillin Aerosol Therapy in Sinusitis, Ann. Otol., Rhin. & Laryng. **58**:189-199, 1949.

19. Van Alyea, O. E., and Donnelly, A.: Intranasal Medication with Vasoconstrictors, Arch. Otolaryng. **49**:234-235 (Feb.) 1949.

20. Packard, L. A.: Tyrothricin in the Treatment of Chronic Rhinopharyngitis and Allergic Rhinitis, Eye, Ear, Nose & Throat Monthly **28**:75-78, 1949.

21. Mill, W. A.: The Use and Abuse of Vasoconstrictors in the Nose, Practitioner **162**:160-161, 1949.

22. Fabricant, N. D.: The Overmedicated Nasal Cavity, Am. J. M. Sc. **217**:462-465, 1949.

23. Brem, J., and Zonis, J.: Intranasal Application of Buffered Tripelennamine (Pyribenzamine) Solution in Allergic Rhinitis, J. Allergy **20**:70-73, 1949.

24. Saylor, B. W.: Treatment of Allergic and Vasomotor Rhinitis with Hesperidin Chalcone Sodium, Arch. Otolaryng. **50**:813-820 (Dec.) 1949.

25. Baird, K. A.: Sinusitis, Allergy and Bacterial Vaccine, Ann. Allergy **7**:339-345, 1949.

26. Clein, N. W.: Allergy and the Tonsil Problem in Children, Ann. Allergy **7**:329-333, 1949.

27. Feingold, B. F.: Tonsillectomy in the Allergic Child, California Med. **71**:341-344, 1949.

regrowth occurred in 23 per cent. Feingold feels that edema is the chief factor in enlargement of the tonsils in allergic disease. In the absence of infection removal is indicated only if necessary to relieve obstruction. In cases of infection, removal is indicated unless tonsillar involvement subsides under allergic management alone.

Cutler, Marcus and Lederer [28] report 25 cases of children 4 to 9 years old and two of adults with allergies or an allergic background in whom considerable improvement in nasal and eustachian tube ventilation was obtained by radiation treatment of the nasopharynx by means of Crowe's nasal applicator. Schulz and Robbins,[29] however, warn against possible untoward delayed effects from this procedure.

HAY FEVER

Lazarowitz [30] has written on hay fever as a public health problem. He points out the great economic loss resulting from this condition which involves some 3,000,000 people in the United States for at least six weeks of the year and predisposes them to the development of seasonal asthma, of which there are probably at least 500,000 cases in this country. Lazarowitz feels that early treatment could prevent much of this economic loss.

Durham [31] presents a survey of air-borne allergens in the national parks which should be of value in directing patients to suitable vacation sites. He concludes that the Everglades and Island Royal are the only parks east of the Rocky Mountains suitable as refuges from ragweed pollen. Glacier Park is somewhat better than the parks in Colorado, Utah or Arizona because of the sagebrush in the latter areas. The parks in California, Oregon, Washington and Alaska are almost or entirely free of ragweed and sagebrush. Grass pollens are likely to be encountered in all national parks.

The possibilities of pollen dissemination have been studied by Heise and Heise,[32] who have investigated the distribution of pollens and molds in the upper atmosphere, conducting their studies from an airplane, and Sack,[33] who has collected pollen on slides exposed on ships as far as 200 miles from land.

Heise [34] suggests algae as a possible cause of hay fever symptoms and presents one case in which symptoms were aggravated by swimming in a lake and another in which there were hay fever symptoms and no demonstrable pollen sensitivity. An antigen prepared from the offending algae was effective in the relief of symptoms in both instances.

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28. Cutler, M. H.; Marcus, R. E., and Lederer, F.: Evaluation of the Effects of Radiation on Non-Malignant Lesions of the Nasopharynx, Radiology **52**:816-818 1949.

29. Schulz, M. D., and Robbins, L. L.: Dangers of Irradiation of Hypertrophied Lymphoid Tissue of the Nasopharynx, Tr. Am. Acad. Ophth. **53**:243-253, 1949; Potential Hazards from Radiation Treatment of Hypertrophied Lymphoid Tissue in the Nasopharynx, Laryngoscope **59**:147-155, 1949.

30. Lazarowitz, L. C.: Hay Fever as a Public Health Problem, New York J. Med. **49**: 1960-1962, 1949.

31. Durham, O. C.: Air-Borne Allergens in the National Parks, J. Allergy **20**:255-268, 1949.

32. Heise, H. A., and Heise, E. R.: The Influence of Temperature Variations and Winds Aloft on the Distribution of Pollens and Molds in the Upper Atmosphere, J. Allergy **20**:378-382, 1949.

33. Sack, S. S.: How Far Can Wind-Borne Pollens be Disseminated? J. Allergy **20**:453-460, 1949.

34. Heise, H. A.: Symptoms of Hay Fever Caused by Algae, J. Allergy **20**:383-385, 1949.

The treatment of hay fever has received considerable attention during the past year. Budd and Freeman [35] point out that any extract of a pollen necessarily contains a heterogenous mixture of proteins, of which some are specific for each given species, some for groups of plants, and some are of still wider distribution. They feel that it is necessary to separate these protein fractions to evaluate accurately a patient's sensitivities. Electrophoresis is suggested as a method for accomplishing this separation. Becker and Munoz [36] have been able to demonstrate at least five different antigens in ragweed pollen extracts.

Feinblatt and Love [37] have shown effective absorption of orally administered pollen antigens by means of controlled passive transfer tests. They have demonstrated an effective equivalent of 1,000 pollen units following oral administration of 90 mg. of mixed antigens.

In a discussion of the treatment of hay fever in children, Nevius [38] presents a detailed schedule of doses for desensitization. He considers skin tests highly valuable in these cases. Southwell [39] also considers skin tests valuable in hay fever although of questionable importance in asthma. He too presents a schedule of doses which is itemized for various different pollens. Southwell is af the opinion that a preseasonal desensitization program timed to permit the patient to tolerate the highest dosage at the onset of his hay fever season is best. He considers the antihistaminics of value for symptomatic treatment and does not feel there is much to choose between in the various available drugs.

The use of antihistaminics in conjunction with pollen therapy is discussed by Schulman and Fuchs [40] and Maietta.[41] Schulman and Fuchs used prophenpyridamine (trimeton®) in conjunction with immunization. They also tried iron as an adjunct to this program but found it of no value. Maietta [41] has been able to administer massive doses of pollen antigens to 45 sensitive patients by combining the injection with the administration of antihistaminics. He feels that in this way a high degree of tolerance can develop and the number of required injections be materially reduced.

Dickstein [42] has tried substituting antazoline (antistine®) in 100 to 200 mg. doses for 25 to 50 mg. doses of diphenhydramine or tripelennamine. In 17 highly sensitive patients at the height of the ragweed season the antazoline proved less effective than the other drugs. Dickstein suggests that the change may nevertheless be of value in children or in adults who are highly reactive to drugs. The local use

35. Budd, E., and Freeman, J.: Allergic Specificity of Pollens, Lancet **2**:1171-1172, 1949.

36. Becker, E. L., and Munoz, J.: Multiplicity of Antigens in Ragweed Pollen Extracts as Demonstrated by the Technic of Oudin, Proc. Soc. Exper. Biol. & Med. **72**:287-289, 1949.

37. Feinblatt, T. M., and Love, R.: Oral Pollen Absorption Demonstrated by Controlled Passive Transfer Tests, Ann. Allergy **7**:228-231, 1949.

38. Nevius, W. B.: Management of the Child with Hay Fever and Asthma, J. M. Soc. New Jersey **46**:17-22, 1949.

39. Southwell, N.: Treatment of Hay Fever, Practitioner **162**:148-151, 1949.

40. Schulman, P. M., and Fuchs, A. M.: Clinical Studies with Iron as Adjunct to Pollen Immunization and Antihistaminic Therapy in Hay Fever, J. Allergy **20**:444-448, 1949.

41. Maietta, A. L.: Unusually Good Results in Pollinosis with Combined Antigenantihistamine Therapy: Shortening the Treatment of Hay Fever, Ann. Allergy **7**:789-798, 1949.

42. Dickstein, B.: The Effect of Substitution of Antistine (Phenyl-Benzyl-Amino-Methyl-Imidazoline) for Benadryl or Pyribenzamine During the Height of the Ragweed Pollen Season, Ann. Allergy **7**:250-253, 1949.

of tripelennamine in hay fever has been suggested by Zeller [43] and Schwartz and Leibowitz.[44] Zeller reports that a 1 per cent solution used as drops gives effective relief. Schwartz and Leibowitz used a 0.5 per cent isotonic buffered solution and recommend an atomizer for its application, thus avoiding a burning sensation complained of after the drops. In both papers the absence of side effects is emphasized.

Brown and Ruskin [45] have reported definite improvement in 60 patients treated with ascorbic acid in doses of 250 mg. three to four times a day. Brown obtained good results in 50 per cent of his patients and Ruskin in 75 per cent.

Russell [46] believes that relatively small areas of the nasal mucosa may be sensitive to inhalants and that injection into these areas of 70 per cent alcohol with the patient under local anesthesia can give immediate complete or partial relief from the symptoms of hay fever for one or more seasons. He considers the presence of inflammation in the teeth or sinuses a contraindication to this method of treatment.

EAR

Ashley [47] feels that allergy may be a much more frequent etiological factor in deafness than is usually recognized. He points out that the eustachian tube and middle ear are subject to the same allergic changes as are the nose and paranasal sinuses. He further believes that the management effective in the treatment of nasal allergies should benefit the ear as well. The examination of nasal mucus for eosinophils is considered as the most valuable test available for confirming a diagnosis of nasal allergy. Biopsies of lymphatic tissue examined for eosinophils may also be useful. Ashley feels that a very high percentage of all children with allergic nasal symptoms have hearing defects and that inhalant and food sensitivities can often be responsible for irreversible changes. The early treatment of allergic manifestations in infants and children should thus prevent much adhesive deafness as well as asthma and asthmatic bronchitis. Treatment is considered as mainly a matter of prophylaxis.

Harrill [6] mentions some of the allergic ear conditions in his review of allergies as seen by the otorhinologist. Skin, middle and inner ear involvement (including Ménière's or Ménière-like conditions) is mentioned.

Allergic otitis externa is mentioned by Rees,[48] who considers identification and avoidance of the allergen the most satisfactory treatment.

Peik, High and Campbell [49] discuss streptomycin toxicity of the eighth nerve. In 21 patients treated with 2 Gm. of dihydrostreptomycin daily for 120 days, all had vestibular dysfunction but none had loss of hearing. Eleven months after

43. Zeller, M.: Nasal Pyribenzamine for Relief of Hay Fever, Ann. Allergy **7**:103-104, 1949.

44. Schwartz, E., and Leibowitz, H.: Local Nasal Therapy with Pyribenzamine in Seasonal and Nonseasonal Hay Fever, J. Allergy **20**:269-272, 1949.

45. Brown, E. A., and Ruskin, S. L.: The Use of Cevitamic Acid in the Symptomatic and Coseasonal Treatment of Pollinosis, Ann. Allergy **7**:65-70, 1949.

46. Russell, B.: Treatment of Hay-Fever by Injection of Nasal Mucosa with Alcohol, Lancet **1**:1098-1099, 1949.

47. Ashley, R. E.: Medical Care and Prophylaxis in Hearing Losses with Special Attention to Allergies, Ann. Otol., Rhin. & Laryng. **58**:837-846, 1949.

48. Rees, C. W.: Otitis Externa, California Med. **70**:288-291, 1949.

49. Peik, D. J.; High, H., Jr., and Campbell, P. A.: Streptomycin Toxicity of the Eighth Nerve, Arch. Otolaryng. **50**:251-254 (Sept.) 1949.

cessation of treatment, four had normal responses to caloric tests and were free of vertigo. None of the others were incapacitated.

MÉNIÈRE'S DISEASE

A good deal has been written on this condition during the past year, particularly in connection with its etiology and surgical treatment.

Williams [50] has reviewed Ménière's original papers and concluded that Ménière had a better conception of the disease than did many otologists who followed him. Williams points out, among other things, that Ménière did not describe hemorrhage into the otic capsule.

In an etiological study of Ménière's disease Selfridge [51] defends the thesis that the condition is related to disturbances of nutrition and thus of body chemistry. The possible role of vitamin deficiency and allergy is discussed. A review of the literature has led him to the opinion that most favorable results in treatment follow the use of several vitamins. Thiamine, nicotinic acid and a member of the group of choline compounds are suggested. Other therapeutic measures mentioned include restricted salt diet and surgical section of the vestibular nerve.

Atkinson [52] has published two papers on vitamin deficiency as the causative factor in Ménière's disease. The first of these papers deals with vestibular disturbance and the second with cochlear disturbance. The vestibular disturbance is thought to be of two types, rotational and positional. Patients with rotational vertigo seem to have a nicotinic acid deficiency. They show, among other things, a small response to intradermal administration of histamine. Nicotinic acid relieves their attacks. In patients with positional vertigo there is a large response to histamine, and the attacks are relieved by riboflavin. Finally, patients may show both kinds of vertigo and an intermediate histamine response. They require both nicotinic acid and riboflavin for the relief of attacks. This last group is the largest one. In the same way the cochlear involvement may be of two types, and the patient may show a perceptive deafness with nicotinic acid deficiency, a conductive deafness with riboflavin deficiency or a type of mixed deafness with a combined deficiency.

M. R. Brown [53] discusses the possibility of a hereditary factor in Ménière's disease. Five families in each of which two cases occurred are reported. The affected members of two more families, including three siblings, children of first cousins and identical twins, are reviewed. Her conclusion is that Ménière's disease appears to be an inherited disorder.

The allergic etiology of endolymphatic hydrops is considered as proved in certain cases reported by Fischer [54] in a general review of the subject of vertigo.

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50. Williams, H. L.: A Review of Ménière's Original Papers in the Light of Our Present Knowledge of Ménière's Disease, Ann. Otol., Rhin. & Laryng. **58**:761-770, 1949.

51. Selfridge, G.: Ménière's Symptom Complex: Its Relation to Chemistry; An Etiologic Study, Arch. Otolaryng. **49**:1-15 (Jan.) 1949.

52. Atkinson, M.: Ménière's Syndrome: Observations on Vitamin Deficiency as the Causative Factor; I. The Vestibular Disturbance, Arch. Otolaryng. **49**:151-174 (Feb.) 1949; II. The Cochlear Disturbance, ibid. **50**:564-588 (Nov.) 1949.

53. Brown, M. R.: The Factor of Heredity in Labyrinthine Deafness and Paroxysmal Vertigo (Ménière's Syndrome), Ann. Otol., Rhin. & Laryng. **58**:665-670, 1949.

54. Fischer, J. J.: Otologic Aspects of Vertigo, New England J. Med. **241**:142-144, 1949.

Evans [55] reports a case which followed a caisson accident. In this instance hemorrhage into the labyrinth was suggested as the cause. Evans claims that trauma is now accepted as a possible cause of Ménière's disease. It is interesting to note that a third nerve palsy followed alcohol destruction of the labyrinth in Evans' case.

The surgical treatment of Ménière's disease has been reviewed in some detail by Lindsay,[56] Lathrop [57] and Altmann.[58] Lindsay has described and evaluated the various surgical procedures available. For the attainment of the ideal result, namely the relief of vertigo and the preservation of hearing, none of them is entirely satisfactory. For instance, Portmann's operation on the saccus endolymphaticus preserves hearing but is not effective enough in the relief of the vertigo. Ablation of the ampullary end of the horizontal semicircular canal prevents the vertigo but interferes with hearing. Labyrinthine decompression is not considered effective. Coagulation of the labyrinth Lindsay believes offers the most hope of preservation of hearing with the control of vertigo. All surgical procedures are considered as last resort measures to be used when other methods have failed.

According to Lathrop,[57] the ideal operation for Ménière's disease is selective section of the eighth nerve. Certain disadvantages of this operation are, however, indicated, especially the questionable benefit of preserving a distorted remnant of hearing. Lathrop concludes that the operation is best in patients with good bilateral hearing and evidences of bilateral disease. He points out that in 44 patients treated by selective eighth nerve section, audiometric tests showed "practical" hearing in the affected ear in only 13. For these reasons the more easily executed operations on the inner ear are probably preferable. Lathrop does not feel that there is much to choose between in avulsion of the membranous horizontal semicircular canal or electrocoagulation of the canal and the vestibule.

Altmann [58] is of the opinion that in true Ménière's disease medical treatment holds little promise, although he states that it should be tried. Of surgical procedures, he considers decompression of the labyrinth unsatisfactory. Drainage can be used in all cases but is not particularly successful in many. It is considered most useful under circumstances in which preservation of hearing is essential. Section of the eighth nerve is not considered better than the less hazardous labyrinthine procedures. Other methods discussed include surgical treatment of the autonomic nervous system.

Day and Lindsay [59] report a case in which the coagulation operation had been performed five years previously. In this case the result had been good, and some hearing had been preserved.

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55. Evans, J.: An Unusual Case of Ménière's Disease, J. Laryng. & Otol. **63**:311-313, 1949.

56. Lindsay, J. R.: Labyrinthine Surgery for Ménière's Disease, Laryngoscope **59**:22-34, 1949.

57. Lathrop, F. D.: Surgery of Ménière's Syndrome: Evaluation of Neurosurgical and Otologic Procedures, Ann. Otol., Rhin. & Laryng. **58**:809-822, 1949.

58. Altmann, F.: Surgical Treatment of Ménière's Disease, Laryngoscope **59**:1045-1067, 1949.

59. Day, K. M., and Lindsay, J. R.: Hydrops of the Labyrinth: Case Report; Coagulation Operation, Clinical Course and Histopathology, Laryngoscope **59**:213-227, 1949.

Denny-Brown [60] believes that there are definite disadvantages to surgical treatment of Ménière's disease and that surgery should be resorted to only when the patient is incapacitated and his livelihood is at stake.

Witzeman [61] has suggested the use of dimenhydrinate (dramamine®) in vertigo, recommending 50 mg. doses three to four times daily and up to as much as 800 mg. in 24 hours if necessary.

EYE

Woods [62] has presented a thorough discussion of ocular allergy with a description of the different types of allergic reactions. The anaphylactic, or pollen, type and the bacterial type are clearly described and differentiated. A large number of conditions are included. Under the heading conjunctiva are given the sudden edematous types of reaction, the eczematous edematous type of blepharoconjunctivitis, chronic or recurrent irritative conjunctivitis and vernal catarrh. Under cornea, phlyctenular keratoconjunctivitis and marginal ulcers are listed. Under uveal tract are those conditions thought to be due to native organ-specific proteins of the eye. They include sympathetic ophthalmia (sensitization to uveal pigment) and endophthalmitis phacoanaphylactica (sensitization to lens protein). Nongranulomatous and granulomatous uveitis are also listed. The former is due to bacterial invasion. Methods for establishing responsible allergens are discussed. Woods feels that skin tests are of value but that the ophthalmic test is both unreliable and hazardous. He does not believe that food allergy is often responsible for ophthalmic disturbances, and hence the field is narrowed essentially to air-borne allergens, organ-specific substances and bacteria. Treatment is discussed under the headings isolation, desensitization and adjuvants. Among the latter are included the antihistamine drugs and beta radiation for vernal catarrh. Desensitization with uveal pigment (which is not considered as of much value) and lens protein is discussed.

Gill [63] also gives a general discussion of ocular allergy including many of the same conditions. He mentions cytological examination of secretions of the eye as a definite aid to diagnosis in some, but not all, allergic conditions.

According to Braley [64] the diagnosis and treatment of uveitis have proved to be both uncertain and discouraging. He has inoculated anterior chamber fluid from 20 eyes with uveitis into the eyes of mice and into tissue cultures and recovered the infective agent. Ground tissue from the irises and ciliary bodies of five eyes enucleated because of uveitis failed to reveal any organisms when inoculated into mice, guinea pigs and rabbits. Braley considers bacterial allergy the most important cause of uveitis. He believes that typhoid vaccine is still the treatment of choice and points out that antibiotics and antihistaminics have proved ineffective.

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60. Denny-Brown, D. E.: Neurologic Aspects of Vertigo, New England J. Med. **241**:144-145, 1949.

61. Witzeman, L. A.: A New Treatment for Vertigo, Eye, Ear, Nose & Throat Monthly **28**:272-273, 1949.

62. Woods, A. C.: The Diagnosis and Treatment of Ocular Allergy, Am. J. Ophth. **32**:1457-1478, 1949.

63. Gill, W. D.: Ocular Allergy: Allergic Phenomena Affecting the Eye and Its Adnexa, Arch. Ophth. **42**:238-248 (Sept.) 1949.

64. Braley, A. E.: The Etiology and Treatment of Uveitis, J. Iowa M. Soc. **39**:57-60, 1949.

In a discussion of 61 cases of sympathetic ophthalmia, McPherson [65] does not mention allergy as a possible etiological factor.

Allen [66] discusses blepharoconjunctivitis and states that the manifestations of the allergic form may vary from slight itching to severe vesiculation and excoriation of the skin. He recommends removal of the offending allergen when possible and the use of the antiallergic drugs.

Wilkins [67] has briefly reviewed phlyctenular keratoconjunctivitis, which he believes is usually the result of a sensitivity to an endogenous toxin or protein developing in the corneal and conjunctival epithelium.

A case of bilateral neuroretinitis and cyclitis following a routine intracutaneous test with 0.1 mg. of old tuberculin in a healthy man is reported by Weizenblatt.[68] The reaction persisted several weeks. Six and a half years later the same man, again tested with tuberculin, manifested a similar reaction. He had been free of all ocular symptoms during the interval.

Other ocular allergies reported include a case in which there was diminution of visual fields apparently due to spasm in the choroidal arteries. The patient recovered after the elimination of pork and tobacco. He also had migraine which was controlled with the same regimen (Zussman [69]).

Cowan [70] describes a case of sensitivity to tetracaine (pontocaine®) instilled locally, and Forster and Dickey [71] report a case of sensitivity to a gold ball orbital implant.

Leopold, Dean and Blazar [72] have tried tripelennamine as a therapeutic and prophylactic agent in experimental uveitis in rabbits. They found that uveal inflammation was prevented only if the drug was given before the shocking dose of protein. The condition was not cleared by tripelennamine administered after the shocking dose. It is suggested that antihistamine drugs may be of value in the prevention but not the treatment of anaphylactic ocular hypersensitivity reactions.

Fralick and Kiess [73] have found that contact dermatitis and conjunctivitis may occasionally follow the use of atropine and that by using tripelennamine orally or diphenhydramine locally they were able to continue the atropine in nine such cases.

Daily and Daily [74] used a combination of 0.5 per cent antazoline and 0.025 per cent naphazoline (privine®) instilled into the conjunctiva in 100 patients with

65. McPherson, S. D., Jr.: Sympathetic Ophthalmia, South. M. J. **42**:120-124, 1949.

66. Allen, J. H.: Diagnosis and Treatment of Blepharoconjunctivitis, J. Iowa M. Soc. **39**:5-8, 1949.

67. Wilkins, W. T.: Phlyctenular Kerato Conjunctivitis, Mississippi Doctor **27**:297-299, 1949.

68. Weizenblatt, S.: Allergic Ocular Reaction to the Tuberculin Test, Arch. Ophth. **41**:436-443 (April) 1949.

69. Zussman, B. M.: Allergy of the Eye Associated with Migraine Headache, Ann. Allergy **7**:524-527, 1949.

70. Cowan, T. W.: Sensitivity to Pontocaine Instilled Locally, Am. J. Ophth. **32**:263-264, 1949.

71. Forster, H. W., Jr., and Dickey, R. F.: A Case of Sensitivity to Gold Ball Orbital Implant, Am. J. Ophth. **32**:659-662, 1949.

72. Leopold, I. H.; Dean, W., and Blazar, H.: An Evaluation of an Antihistaminic Drug in Experimental Uveitis, Am. J. Ophth. **32**:31-34, 1949.

73. Fralick, F. B., and Kiess, R. D.: Use of Antihistaminic Drugs in Control of Atropine Dermatitis and Conjunctivitis, Arch. Ophth. **41**:583-586 (May) 1949.

74. Daily, R. K., and Daily, L., Jr.: Use of Privine-Antistine Drops in Ophthalmology, Am. J. Ophth. **32**:441-442, 1949.

various kinds of conjunctivitis. They obtained relief from the burning, itching, photophobia and lacrimation, and the congestion and blepharospasm in allergic conjunctivitis were reduced. A general discussion of antihistamines in ophthalmology has been published by Nemeth.[75]

HEADACHE

Braaf [76] has clearly stated a series of criteria distinctive of true migraine. These include head pain that is usually one sided, periodic attacks, gastrointestinal symptoms, indications of cortical disturbances such as paresthesias and scotomas and relief by use of ergotamine tartrate (gynergen®). Twenty patients showing the first two criteria and at least two showing the other three were treated by head traction and manipulation and the administration of thiamine hydrochloride intramuscularly. Treatment was continued from one to 12 weeks and proved successful. Braaf believes the cause of the attacks was herniation of cervical intervertebral disks with compression of the first two cervical nerves.

Marcussen and Wolff [77] are of the opinion that many of the prodromal phenomena in migraine are associated with intracranial vasoconstriction and that vasodilators will abolish these symptoms and may at times abort attacks. The headache itself is thought to be due to painful vasodilatation of the cranial arteries. Ergotamine tartrate is considered the drug of choice at this stage and is most effective when given at the onset of the headache. Emotional factors are evaluated in the etiology of migraine, and it is concluded that their adjustment can materially reduce the frequency and severity of attacks.

Podolsky [78] particularly emphasized mental hygiene and psychotherapy in the treatment of migraine. Waldbott,[79] on the other hand, enters a plea for allergic management of migraine, with consideration of psychosomatic relations as of secondary importance.

Hackzell, Kraepelien and Vahlquist,[80] however, have submitted 40 patients with typical migraine to allergic analysis and have concluded that their investigation did not support the theory that allergy is a common cause of migraine.

Allergy is believed to be the cause of nuchal myalgia and associated headache by Randolph,[81] who has demonstrated specific inhalants and foods to be inciting agents. He is of the opinion that involvement of the neck muscles is the most frequently encountered manifestation of allergy affecting skeletal musculature and that there is no evidence that such symptoms are to be explained on a psychosomatic basis.

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75. Nemeth, L.: Antihistamines in Ophthalmology, Brit. J. Ophth. **33**:665-669, 1949.

76. Braaf, M. M.: Migraine Headache Treated Successfully by Head-Traction, Manipulation and Thiamin Chloride, New York J. Med. **49**:1812-1816, 1949.

77. Marcussen, R. M., and Wolff, H. G.: Therapy of Migaine, J. A. M. A. **139**:198-200 (Jan. 22) 1949.

78. Podolsky, E.: The Treatment of Migraine, M. Rec. **162**:11-12, 1949.

79. Waldbott, G. L.: Migraine, J. A. M. A. **139**:734 (March 12) 1949.

80. Hackzell, G.; Kraepelien, S., and Vahlquist, B.: Migraine and Allergy, Acta allergol. **2**:95-104, 1949.

81. Randolph, T. G.: Allergy as a Cause of Nuchal Myalgia and Associated Headache, Arch. Otolaryng. **50**:745-758 (Dec.) 1949.

Hansel [82] and Cohen and Criep [83] discuss the use of ergotamin with caffeine (caffergone®) in the treatment of headache. Hansel [82] reports that the usefulness of ergotamine with caffeine is much more general than the treatment of migraine alone and that it is of special value in typical and atypical histamine cephalalgia. Ergotamine tartrate and dihydroergotamine (D.H.E. 45) are considered more reliable than ergotamine with caffeine in migraine if they can be administered at the onset or even during the episode. Cohen and Criep [83] used ergotamine with caffeine in the form of suppositories containing 100 mg. of caffeine and 2 mg. of ergotamine tartrate in the treatment of 50 patients. The patients are reported under the headings of histamine headache (two patients, both relieved), allergic headache (four patients, three relieved) and migraine. There were 44 patients in the migraine group, of whom 13 were described as obtaining marked relief; 17, moderate relief; 5, mild relief; 2, doubtful relief, and 7, no relief.

Peters and Zeller [84] have tried a new drug, methylamino isooctene (octin®) for vasodilation headache. With doses of 2 grains (0.13 Gm.) every 30 minutes (up to the time of relief or the administration of four doses) some relief was afforded in 11 of 21 trial cases of migraine, one case of histamine cephalalgia and three of four cases of tension headache. Results of administration early to abort attacks were somewhat similar.

A case of migraine in which tolerance and refractoriness to the ergot alkaloids developed is described by Wolfson and Graham.[85] This patient was eventually relieved by section of the sensory root of the right trigeminal nerve.

Eszenyi-Halasy [86] discusses the clinical features and possible pathogenesis of histamine headache. Four patients treated with histamine are reported.

ASTHMA

Williams and Williams [87] have reviewed 300 cases of bronchial asthma. They feel that the allergic factor is a very important one, and they point out the importance of hormonal allergy in women. They conclude that there are three combinations of factors producing the asthmatic state: etiological and aggravating, etiological but not aggravating and aggravating but not etiological. In a small series of cases followed over seven to 12 years, 19.4 per cent of the patients are reported fully recovered and 17.2 per cent dead, emphasizing the importance of asthma as a fatal disease.

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82. Hansel, F. K.: The Treatment of Headache, with Particular Reference to the Use of Cafergone (Ergotamine Tartrate and Caffeine) for the Relief of Attacks, Ann. Allergy **7**:155-161, 1949.

83. Cohen, S. G., and Criep, L. H.: Observations on the Symptomatic Treatment of Chronic Vascular Headache with Cafergone (Ergotamine Tartrate with Caffeine), New England J. Med. **241**:896-200, 1949.

84. Peters, G. A., and Zeller, W. W.: Evaluation of a New Agent (Methyl-Iso-Octenylamine) in the Treatment of Vasodilating Headaches, Proc. Staff Meet., Mayo Clinic **24**:265-268, 1949.

85. Wolfson, W. Q., and Graham, J. R.: Development of Tolerance to Ergot Alkaloids in a Patient with Unusually Severe Migraine, New England J. Med. **241**:296-298, 1949.

86. Eszenyi-Halasy, M.: Histamine Headache, Brit. M. J. **1**:1121-1123, 1949.

87. Williams, E. O., and Williams, G. E. O.: The Natural History of Asthma: A Review of 300 Cases, Brit. M. J. **2**:897-900, 1949.

Davison [88] has reviewed 100 charts of unselected patients who had undergone bronchoscopy. Forty-nine of these proved to be atopic. Twenty of the 49 had bronchiectasis, 15 chronic bronchitis, 10 asthma and chronic bronchitis and 4 allergic pulmonary consolidation. Of the patients with bronchiectasis, 76 per cent were allergic. The high incidence of allergy in chronic bronchitis and bronchiectasis, Davison believes, emphasizes the importance of allergic management in such cases.

Lister [89] is of the opinion that chronic bronchitis is not a complete diagnosis; that the term rather covers a sort of "waste basket" group of cases. He believes that allergic bronchial spasm (asthma) is the essential element in the entire group and that infection is generally secondary.

Kaye, Whittenberger and Silverman [90] have studied the air flow pattern in subjects of various ages and under various conditions, using a face mask diaphragm and recording photographically. In children during asthmatic attacks they found that the expiratory flow fell to a low velocity after the peak flow. Oscillations normally superimposed on the basic variations were lost. These variations were typical and uniform in successive cycles. Normal patterns occurred between attacks in some children. In adults with pulmonary complications of asthma, such as emphysema, the tracings were sometimes abnormal between attacks. Abnormal tracings were also reported in bronchiectasis, kyphoscoliosis and pulmonary disease with fibrosis of the pancreas.

The respiratory air-flow pattern has also been studied in asthmatic and normal persons by Proctor and Hardy [91] and recorded in the form of the "pheumotachogram," a continuous record of the alterations in velocity of the air flow at the nose or mouth during respiration.

Jennes [92] after a series of vital capacity studies on asthmatic persons felt that this method might aid in the differentiation of the extrinsic (nonbacterial or immunologic) type from the intrinsic (bacterial or nonimmunologic) type. Patients in the extrinsic group showed less diminution of vital capacity and greater tendency to return to normal between attacks than did those in the intrinsic group. Both groups were found to be adversely affected by symptoms of long duration.

In studies of electrocardiographic tracings from 50 asthmatic persons, Rom and Jend [93] conclude that changes due to bronchial asthma are not common. Forty-four of their patients revealed no changes which could be interpreted as indicating myocardial damage due to asthma.

The significance of mediastinal shift in asthma is discussed by Osmond,[94] who feels that observation (fluoroscopic or inspiratory and expiratory films) is essential in the diagnosis and treatment of complications such as bronchial occlusion.

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88. Davison, F. W.: Bronchopulmonary Infections in Allergic Individuals, Ann. Otol., Rhin. & Laryng. **57**:884-893, 1949.

89. Lister, W. A.: Chronic Bronchitis, Never a Complete Diagnosis, Lancet **1**:719-721, 1949.

90. Kaye, R.; Whittenberger, J. L., and Silverman, L.: Respiratory Air Flow Patterns in Children, Am. J. Dis. Child. **77**:625-641 (May) 1949.

91. Proctor, D. F., and Hardy, J. B.: Studies of Respiratory Air Flow: 1. Significance of the Normal Pneumotachogram, Bull. Johns Hopkins Hosp. **85**:253-280, 1949.

92. Jennes, S. W.: Vital Capacity Studies to Differentiate Types of Bronchial Asthma, J. Allergy **20**:322-327, 1949.

93. Rom, J., and Jend, W., Jr.: Electrocardiographic Studies in Bronchial Asthma, J. Allergy **20**:428-433, 1949.

94. Osmond, L. H.: Significance of Mediastinal Shift in Asthma, Ann. Allergy **7**:799-806, 1949.

Grossman and Cramer [95] report a case of mediastinal emphysema in a 19 year old patient with asthma. The emphysema was demonstrated roentgenologically and cleared up in two weeks of treatment of the asthma. Two cases of subcutaneous emphysema complicating asthma are reported by Chester.[96] In each case the severe symptoms of asthma abated when the emphysema occurred.

Gelfand [97] describes a case in which the eighth, ninth and tenth ribs were spontaneously fractured during a paroxysm of coughing of an asthmatic patient. He and his associates [98] present another case in which death occurred shortly after the administration of first 1 Gm. of procaine intravenously in 500 cc. of isotonic sodium chloride solution and later amobarbital (amytal®) sodium.

The temporary relief of intractable asthma in three patients following the onset of jaundice is reported by Gorin.[99]

Waldbott,[100] in a discussion of the treatment of asthma, divides the problem into four phases—(1) the emergency, (2) the chronic asthmatic state, (3) the state of rehabilitation and (4) the complications. The emergency treatment is largely a matter of giving of epinephrine, with intravenous administration of aminophylline and antihistaminics. Treatment during the chronic asthmatic state involves prevention of contact with allergens, hyposensitization, control of infection, measures to eliminate allergens from the lungs (by expectorants) and symptomatic treatment. During the state of rehabilitation the psychosomatic element must be considered. The nutrition of the patient is important. Exertion, cold sensitivity and climate must be thought of. Measures dealing with the complications, such as atelectasis, bronchiectasis, pneumonitis and so on, are discussed.

Wittich [1] has also outlined available measures for the treatment of asthma. In status asthmaticus he employs antibiotics in aerosol form with epinephrine or isopropylarterenol (isuprel®). Sedation is considered of paramount importance. The use of an oxygen and helium mixture is mentioned. In less acute cases the treatment is variable and includes epinephrine or ephedrine. X-ray treatment is thought to benefit perhaps a fourth of selected cases. Other measures mentioned include vaccine therapy, surgical procedures and consideration of psychomatic factors. Dust-seal® to keep down possible inhalant allergens is considered a helpful measure.

In status asthmaticus McLaughlin and Parkhurst [101] recommend the following measures: (1) hospitalization if possible; (2) epinephrine (1:1,000), 1 cc. admin-

95. Grossman, J. W., and Cramer, O. S.: Mediastinal Emphysema Occurring During an Acute Paroxysm of Bronchial Asthma, Radiology **52**:705-706, 1949.

96. Chester, S. W.: Subcutaneous Emphysema Complicating Chronic Bronchial Asthma, Ann. Allergy **7**:783-784, 1949.

97. Gelfand, M. L.: Spontaneous Rib Fracture in Bronchial Asthma, Ann. Allergy **7**:217-218, 1949.

98. Gelfand, M. L.; Mufson, M. H., and Richman, W. P.: Death in a Case of Bronchial Asthma Treated Successively with Intravenous Procaine and Sodium Amytal, New York J. Med. **49**:2841-2842, 1949.

99. Gorin, N.: Temporary Relief of Asthma by Jaundice, J. A. M. A. **141**:24-25 (Sept. 3) 1949.

100. Waldbott, G. L.: New Trends in the Treatment of Allergic Diseases, J. Michigan M. Soc. **48**:1140-1143, 1949.

101. McLaughlin, J. S., and Parkhurst, L. W.: The Management of Severe Intractable Asthma (Status Asthmaticus), M. Clin. North America **33**:1597-1603, 1949.

istered subcutaneously, 0.25 cc. every hour afterward; (3) aminophylline, 0.5 Gm. intravenously in 20 cc. isotonic sodium chloride solution every six hours or continuously in 1,000 cc. of 75 per cent dextrose; (4) potassium iodide, 10 grains (0.65 Gm.) three times a day; (5) oxygen via nasal tube; (6) caffeine and sodium benzoate, 0.5 Gm. intramuscularly to be repeated in four hours; (7) intravenous administration of fluids; (8) ether and oil given by rectal tube, and (9) phenobarbital, 0.5 grain (0.03 Gm.) three times a day. Of these, the physician must select the items best suited to the needs of any particular patient.

Nevius [38] believes that ephedrine and epinephrine are still the drugs of choice in asthma in childhood. Ethyl-nor-epinephrine (butanfrine®) may be a useful substitute, and aminophylline in doses of 0.25 Gm. intravenously may be helpful. He particularly emphasizes the importance of environmental control and hyposensitization.

Heise [102] has found filtrates prepared from alpha streptococci recovered from sputums of asthmatic persons to be powerfully antigenic in producing bronchial asthma and effective in high dilutions in its treatment, especially in chronic asthma in children. The filtrates are not effective on inhalant asthma, but it is thought that they may prevent its continuation after removal of the inhalant.

Blatt and Nantz [103] report 17 cases of bacterial asthma treated with sterile broth filtrates of bacteria to which the patients were sensitive. The cases of two of these patients who had remained asymptomatic on this regimen for several months are described in detail.

Fifty patients with intrinsic and mixed bronchial asthma and associated chronic sinusitis treated with autogenous vaccines are reported by Grorud.[104] Results were considered favorable in 37 patients. Best results were obtained early and in patients with little or no roentgenologic evidence of organic changes. Grorud believes that chronic sinusitis is the most important focus of infection in intrinsic asthma and that Staphylococcus aureus is the most important organism.

Hansen-Pruss and King [105] believe that the subject of vaccine therapy in infectious asthma is still in debate and it is probably useful only in selected cases when employed alone. It may be effective after removal of focal infection or after control of infection by antibiotics. Among the antibiotics, streptomycin and penicillin are mentioned, the choice depending on the preponderance of gram-positive or gram-negative organisms. Both antibiotics can be used alternately or together.

Beakey, Bresnick, Levinson and Segal [106] have studied the protective action of various drugs against bronchospasm in asthmatic patients. The decrease in vital capacity induced by methacholine before and after administration of the drug was assayed. Atropine in 0.6 mg. doses given intravenously was found to give complete

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102. Heise, H. A.: The Role of Streptococci in Bronchial Asthma: Etiologic Significance and Treatment with Streptococcus Filtrates, Ann. Allergy **7**:240-249, 1949.

103. Blatt, H., and Nantz, F. A.: Asthma Due to Bacterial Allergy Identified by Tissue Culture and Treated by Desensitization, Ohio M. J. **45**:40-42, 1949.

104. Grorud, A. C.: The Treatment of Intrinsic Bronchial Asthma with Autogenous Vaccine, Ann. Allergy **7**:540-549, 1949.

105. Hansen-Pruss, O. C., and King, H. A.: Chemotherapy and the Use of Vaccine in Infectious Asthma, North Carolina M. J. **10**:175-178, 1949.

106. Beaky, J. F.; Bresnick, E.; Levinson, L., and Segal, M. S.: Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm: III. Anticholinergic Agents, Ann. Allergy **7**:113-121, 1949.

protection for two hours and significant protection for an additional two hours. Bellafoline® (a combination of the malic acid salts of the total levorotatory alkaloids of belladonna leaves) in 0.5 mg. doses gave similar results for three hour periods. When used as an aerosol against aerosolized methacholine (mecholyl®), the protection time was half that obtained with intravenous administration. With scopolamine in 0.3 mg. doses intravenously, protection was complete for two hours and significant for three hours more. Oral administration of scopolamine conferred complete protection for five hours after a one hour latent period. None of the drugs mentioned conferred any protection against histamine. Similar studies (Segal, Levinson, Bresnick and Beakey [107]) on aminophylline showed that 0.5 Gm. given intravenously gave immediate protection against both histamine and methacholine, but the protection in the latter case was below significant limits. In 0.5 Gm. doses rectally the drug was more effective, but there was a delay of 45 to 60 minutes in protection. It was found relatively ineffective on intramuscular and oral administration. Various adrenergic agents were also tested (Bresnick, Beakey, Levinson and Segal [108] and no consistent differences on intravenous or aerosol administration found. The drugs include isopropylartereno, vaponephrin (a solution of synthetic racemic epinephrine hydrochloride) and phenylephrine, as well as epinephrine.

The clinical results of administration of diphenhydramine and tripelennamine intravenously, rectally and as an aerosol to 15 acutely ill asthmatic patients (the condition of eight considered intractable) is reported by Rubitsky and his associates.[109] Significant relief of bronchospasm and prompt restoration of epinephrine sensitivity in 10 of the 15 followed the intravenous treatment. Results were best in patients previously found to be histamine sensitive. They were least satisfactory in patients with bronchial obstruction and cardiac or pulmonary disease. It is concluded that this form of therapy is chiefly valuable in conjunction with other methods in acutely ill patients.

Friedman [110] treated 12 patients with diphenhydramine in aerosol form and reports that all were benefited. Seven of these patients had failed to respond to the systemic administration of antihistamine drugs.

Herxheimer [111] found that promethazine (phenergan) and anthisan, the British term for pyranisamine, would relieve mild bronchial spasm following the administration of allergenic extracts, histamine and methacholine chloride. Severe attacks were not relieved. He believes that clinical evidence indicates the antihistaminics to be of value in mild and moderate asthmatic states. They are best used at night, with other measures in the daytime. Herxheimer feels that the wide variation in response to antihistaminics makes individual determination of dosage necessary.

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107. Segal, M. S.; Levinson, L.; Bresnick, E., and Beakey, J. F.: Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm: VI. Aminophylline, J. Clin. Invest. **28**: 1190-1195, 1949.

108. Bresnick, E.; Beakey, J. F.; Levinson, L., and Segal, M. S.: Evaluation of Therapeutic Substances Employed for the Relief of Bronchospasm: V. Adrenergic Agents, J. Clin. Invest. **28**:1182-1189, 1949.

109. Rubitsky, H. J.; Bresnick, E.; Levinson, L.; Risman, G., and Segal, M. S.: Parenteral and Aerosol Administration of Antihistaminic Agents in the Treatment of Severe Bronchial Asthma, New England J. Med. **241**:853-859, 1949.

110. Friedman, L. L.: The Use of Aerosol "Benadryl" in Bronchial Asthma, South. M. J. **42**:491-492, 1949.

111. Herxheimer, H.: Antihistamines in Bronchial Asthma, Brit. M. J. **2**:901-905, 1949.

Curry, Fuchs and Leard,[112] Roy, Seabury and Johns, [113] S. Friedlaender and A. S. Friedlaender [114] and Schiller and his associates [115] have tried orthoxine® (beta [ortho-methoxyphenyl] isopropylmethylamine hydrochloride) in the treatment of bronchial asthma. This drug has been found to be an effective bronchial dilator not associated with stimulating effects on the central nervous system or a vasodepressor action. Curry and his associates found methoxyphenamine (orthoxine®) in 200 mg. doses equivalent to ephedrine sulfate in 30 mg. doses in protection against experimental reduction in vital capacity. They believe the drug has a definite place in the treatment of asthma. Roy, Seabury and Johns have made spirometric studies on 20 patients with moderately acute attacks of asthma and also have found methoxyphenamine an effective bronchodilator.

The Friedlaenders consider the effective adult oral dose of methoxyphenamine to be 100 to 200 mg. Schiller and his associates treated 50 asthmatic patients ranging in age from 4 to 63 years with methoxyphenamine. They used doses of from 50 mg. in children to 200 mg. in adults. Excellent results were obtained in seven of 14 patients with mild asthma, in 10 of 21 with moderate asthma and in only one of 15 with severe asthma. Seventeen patients had fair results, and 17 experienced no relief. Side reactions occurred in seven (four had gastric disturbances and menstrual-like cramps, dizziness, sleepiness or excessive perspiration).

Results with isopropylarterenol are reported in a number of communications. Lowell, Curry and Schiller [116] have used it as an aerosol and sublingually and subcutaneously. It is regarded as very effective in aerosol form in the relief of mild and moderate asthma but is much less satisfactory in severe and prolonged asthma. After severe episodes it still may be of value in control of subsequent mild attacks. Lipman [117] tried isopropylarterenol on 23 patients with asthma and found that 12 were completely relieved by a single 5 mg. tablet sublingually. Eight others obtained partial or slight relief. Freedom from attacks was maintained in seven of nine patients taking isopropylarterenol orally. The drug was of value in eight persons who were epinephrine fast or subject to side reactions from epinephrine. Isopropylarterenol gave side reactions (palpitation, weakness and nausea) in 14 cases.

Krasno, Grossman and Ivy [118] administered isopropylarterenol sulfate in the form of a dust to 24 patients with asthma. Nineteen responded, and their asthma was controlled by this method; four others are described as giving good response and one was not relieved. Asthma in 16 of the patients was controlled by the dust

112. Curry, J. J.; Fuchs, J. E., and Leard, S. E.: Clinical and Experimental Studies with Orthoxine in the Treatment of Bronchial Asthma, J. Allergy **20**:104-110, 1949.

113. Roy, E. C.; Seabury, J. H., and Johns, L. E., Jr.: Spirometric Evaluation of Orthoxine in Bronchial Asthma, J. Allergy **20**:364-368, 1949.

114. Friedlaender, S., and Friedlaender, A. S.: Observations on the Action of Orthoxine in Patients with Bronchial Asthma, Ann. Allergy **7**:683-688, 1949.

115. Schiller, I. W.; Lowell, F. C.; Franklin, W., and Denton, C.: Orthoxine in Bronchial Asthma: Clinical Evaluation, New England J. Med. **241**:231-233, 1949.

116. Lowell, F. C.; Curry, J. J., and Schiller, I. W.: A Clinical and Experimental Study of Isuprel in Spontaneous and Induced Asthma, New England J. Med. **240**:45-51, 1949.

117. Lipman, W. H.: The Treatment of Bronchial Asthma with Isuprel, Ann. Allergy **7**:384-389, 1949.

118. Krasno, L. R.; Grossman, M. I., and Ivy, A. C.: The Inhalation of 1-(3', 4',-Dihydroxyphenyl)-2-Isopropylaminoethanol (Norisodrine Sulfate Dust), J. Allergy **20**:111-115, 1949.

(norisodrine sulfate dust) alone; eight required aminophylline and iodides. Administration of isopropylarterenol sulfate as a dust is regarded as safe, no serious side effects having been encountered. The dosage consisted of 3 to 5 mg. of dust repeated in half an hour if necessary.

Aminophylline inhaled in particulate form is reported by Taplin, Gropper and Scott [119] to have given symptomatic relief to 30 of 35 persons with asthma. In severe attacks the relief lasted only 30 to 40 minutes but could often be prolonged by repeated doses. It is reported that 60 mg. of aminophylline administered in this way gave immediate average increases of 555 cc., or 21 per cent, in vital capacity. Intravenous administration of aminophylline in 240 to 480 mg. doses gave 786 cc., or 30.9 per cent, increases in vital capacity.

Damray [120] found anthaphylline, a combination of aminophylline and anthallan (1-dibutylaminoethyl-5,6,7-trihydroxy isobenzofuran-[3]-one), more effective than aminophylline alone in relieving asthmatic attacks in 17 patients.

The use of isopropylepinephrine in bronchial asthma is discussed by Gay and Long.[121] They found this drug effective as a bronchodilator when administered orally, subcutaneously, sublingually or by inhalation. Like most other drugs reported, it proved more effective in mild than in severe cases. Side effects are described as palpitation, nausea, headache, nervousness, tremor, dizziness and precordial pain. They occurred in 4 per cent of patients treated by inhalation and in 33 to 100 per cent of patients treated by other routes. In several cases attacks of coronary insufficiency followed the drug.

A number of other measures in the treatment of asthma are discussed. Fogel [122] reports a 38 year old man with intractable status asthmaticus who responded dramatically to intravenous administration of typhoid vaccine. Sheldon [123] discusses the use of fluids intravenously and recommends 5 per cent dextrose in distilled water, up to 3,000 cc. in 24 hours. He condemns the use of saline solution intravenously. Waldbott [124] found the relief afforded 73 of 180 patients by bronchoscopic therapy "somewhat disappointing." However, he considers the method highly valuable as a life-saving measure in extremely chronic cases. Leddy and Maytum [125] report on x-ray treatment in moderate and severe cases of asthma. The method is used only after other measures have failed. They report best results in cases of severe and more constant symptoms and in cases of long duration. Improvement follows treatment by one to two days, and the full effect is apparent in four

119. Taplin, G. V.; Gropper, A. L., and Scott, G.: Micropowdered Aminophylline or Theophylline Inhalation: Therapy in Chronic Bronchial Asthma; Evaluation by Recorded Vital Capacity Changes, Ann. Allergy **7**:513-523, 1949.

120. Damray, F.: Relief of Bronchial Asthma: A Clinical Study with Anthaphylline, M. Rec. **162**:9-12, 1949.

121. Gay, L. N., and Long, J. W.: Clinical Evaluation of Isopropylephinephrine in Management of Bronchial Asthma, J. A. M. A. **139**:452-457 (Feb. 12) 1949.

122. Fogel, M.: Response to Intravenous Typhoid Vaccine in Intractable Status Asthmaticus, New York J. Med. **49**:1170-1172, 1949.

123. Sheldon, J. M.: Intravenous Use of Fluids in Bronchial Asthma, J. A. M. A. **139**:506-507 (Feb. 19) 1949.

124. Waldbott, G. L.: Bronchoscopic Therapy in Allergic Asthma, J. Allergy **20**:335-343, 1949.

125. Leddy, E. T., and Maytum, C. K.: Roentgen Treatment of Bronchial Asthma, Radiology **52**:199-203, 1949.

to five days. Both a high dose (500 r over the mediastinum, both anterior and posterior) and a low dose (250 r) have been used. Untoward results are said to be less frequent with the latter method.

Cohen and Fisher [126] discuss the value of radium treatment of the nasopharynx in asthmatic children. They found that patients with high sedimentation rates benefit more than those with low or normal rates and that results are best in patients with little lymphatic tissue in the nasopharynx and in those with normal sinuses. In general they report that in most cases improvement of symptoms may be expected for about 17 weeks after treatment.

The psychological aspect of the treatment of asthma is discussed by Abramson [127] in conjunction with the various drugs employed. Zoss [128] reports a case of a 19 year old youth suffering from fear of death in whom the anxiety seemed to be a major factor in the cause of asthma. The psychosomatic management of allergic respiratory disease is also discussed by Fischer.[129]

Bruun [130] has shown that while a third of the adult patients with chronic asthma may improve when under the impression that they are receiving rational therapy, 78 per cent will become improved or symptom free under specific desensitization.

The value of breathing exercises in the treatment of asthma is discussed by Dorenson [131] and Levinton and Codon.[132]

Clarke [133] describes excellent results among asthmatic children in Liverpool obtained in a play clinic to which these children were taken as a group.

The literature on bronchial asthma has been covered in a review by Unger and Gordon.[134]

ETIOLOGY

Swineford and Holman [135] have reviewed the question of bacterial allergy and published the results of 3,860 cutaneous tests with 34 crude polysaccharide and nucleoprotein fractions from 14 different bacteria, the preparation of which is

126. Cohen, V. L., and Fisher, W. J.: An Evaluation of Radium Treatment to the Nasopharynx in Asthmatic Children, J. Allergy **20**:328-334, 1949.

127. Abramson, H. A.: Therapy of Asthma with Reference to Its Psychodynamic Pharmacology, Bull. New York Acad. Med. **25**:345-363, 1949.

128. Zoss, S. R.: Anxiety as a Factor in Asthma: A Case Report, Ann. Allergy **7**:785-786, 1949.

129. Fischer, L.: Psychosomatic Management in the Respiratory Allergic Patient, J. M. Soc. New Jersey **46**:516-519, 1949.

130. Bruun, E.: Control Examination of the Specificity of Specific Desensitization in Asthma, Acta allergol. **2**:122-128, 1949.

131. Dorenson, S. M.: Breathing Exercises as an Adjunct in the Treatment of Bronchial Asthma and Pulmonary Emphysema, Am. Pract. **3**:550-554, 1949.

132. Levinton, J., and Codon, A.: Physiotherapy of Asthma: Respiratory Exercises, Acta allergol. **2**:105-112, 1949.

133. Clarke, C. A.: Asthma in Childhood: Experiences in a Liverpool Play Clinic, Practitioner **163**:130-133, 1949.

134. Unger, L., and Gordon, B. F.: Bronchial Asthma: V. Critical Review of Literature, Ann. Allergy **7**:397-431, 1949.

135. Swineford, O., Jr., and Holman, J.: Studies in Bacterial Allergy: I. Introduction; A Brief Critical Review, J. Allergy **20**:292-300, 1949; II. Preparation of Crude Nucleoprotein and Polysaccharide Fractions of Bacteria, ibid. **20**:418-419, 1949; III. Results of 3,860 Cutaneous Tests with 34 Crude Polysaccharide and Nucleoprotein Fractions of 14 Different Bacteria, ibid. **20**:420-427, 1949.

described. They were able to elicit frequent immediate reactions described as indistinguishable from those produced by extracts of foods and inhalants. They also elicited frequent delayed reactions which reached their height in 20 hours. These could not be classified as tuberculin, Arthus or other type of delayed reaction. Swineford and Holman therefore conclude that the use of the term bacterial allergy to designate the tuberculin type of hypersensitivity is probably not correct. They feel that additional diagnostic procedures are needed to establish etiological relations between bacteria and the syndromes of clinical allergy.

Feingold [136] has studied the effects of acute infections on the course of allergy in children. He finds that one group of infections including the viral diseases and pertussis tends to be associated with improvement in the allergy which is aggravated by the other group of infections, those associated in general with leukocytosis.

Dutton [137] has continued the series of studies on molds in the etiology of allergies. He discusses the role of intrinsic molds, otherwise nonpathogenic in the etiology of asthma.

Some of the problems of drug sensitivity have been discussed by Sherman [138] and Hansen-Pruss.[139] Sherman discusses some of the histological lesions of drug sensitivity which may be distinguished from toxic reactions. He mentions arteritis with localized fibrinoid and hyaline degeneration of the media, perivascular infiltration and focal necrosis of the myocardium, spleen, liver and other organs, with mononuclear infiltration. Sherman feels that jaundice may be either a toxic reaction or an allergic reaction and that it is more likely to follow a second course of a drug than the first. Agranulocytosis and thrombopenic purpura are also considered as possible manifestations of drug allergy. It is pointed out that contact sensitization of the skin may be accompanied with generalized sensitization and that reactions may follow either local or oral administration of the drug in question. Skin tests are probably of no value in detecting sensitivities to crystalloids but may aid in the case of protein drugs and vegetable gums. The possible role of vegetable gums in the etiology of allergic reactions attributed to drugs with which they are used is pointed out. Gelfand [140] has studied this last problem at some length and points out that these gums are consumed at the rate of 300 mg. a day per person in the United States. Ingestion experiments with tragacanth, stericula (karaya) gum and acacia on five sensitive patients have established causal relation with allergies. Conditions caused include gastrointestinal allergy, vasomotor rhinitis and bronchial asthma.

Hansen-Pruss [139] discusses the value of various tests in patients suspected of drug allergies. He concludes that a patient suspected of allergy to a drug must be subjected to a series of tests before the suspected sensitivity can be considered as proved or disproved.

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136. Feingold, B. F.: The Influence of Acute Infection upon the Course of Allergy in Children, J. Pediat. **34**:545-558, 1949.

137. Dutton, L. O.: Mold Fungi in the Etiology of Respiratory Allergic Diseases: X. Intrinsic Fungus Factors in Relation to Asthma, Ann. Allergy **7**:585-591, 1949.

138. Sherman, W. B.: Drug Allergy, J. A. M. A. **140**:447-450 (June 4) 1949.

139. Hansen-Pruss, O. C.: Studies of Drug Sensitivity, Ann. Allergy **7**:219-227, 1949.

140. Gelfand, H. H.: The Vegetable Gums by Ingestion in the Etiology of Allergic Disorders, J. Allergy **20**:311-321, 1949.

Penicillin as an allergen has continued to draw considerable attention. Hansel [141] has reviewed the subject and suggested some points on therapy, such as specific immunization with 1 to 2 units of penicillin intradermally every one to two days.

Lepper and his associates [142] have studied the incidence of penicillin reactions in 1,303 patients. They found reactions in 1.2 per cent of 598 patients from penicillin in aqueous solution, in 2.7 per cent of 557 patients from penicillin in oil and wax and in 1.4 per cent of 148 patients from procaine penicillin. With large doses of penicillin in aqueous solution, reactions occurred in 7.8 per cent of the patients. Reactions were more frequent in patients receiving penicillin over long periods and in patients with histories of previous allergies.

In a discussion of penicillin sensitization, Feldman [143] concludes with a plea against the indiscriminate use of this drug.

Haunz and Grinnell [144] have studied the reactions from various preparations of prolonged action in 142 patients. The preparations included penicillin in wax and oil, procaine penicillin in peanut oil and aluminum monostearate and procaine penicillin in aqueous suspension. Eleven of 100 patients given penicillin in wax and oil developed moderate to severe reactions. One mild reaction followed administration of procaine penicillin in oil and none followed the aqueous suspension. It is concluded that the above reactions were due to wax and that administration of calcium penicillin in wax and oil should be discontinued.

Mallen and Cuellar [145] have run immunological studies on the serums of pencillin-sensitive patients which have led them to the conclusion that the demonstrated antibodies developed against the impurities in amorphous penicillin rather than against the crystalline drug.

Cross [146] has reported on oral reaction to penicillin in lozenges, and Samitz and Horvath [147] report two cases of severe penicillin reactions. Waldbott [148] presents a case in which death due to anaphylaxis followed the intramuscular injection of 50,000 units of penicillin, which he feels was accidentally put into a vein.

A case in which desensitization was accomplished by refracted doses of calcium penicillin is reported by Garai.[149]

The development of skin sensitivity to streptomycin by those having contact with this drug is discussed by Simon,[150] who presents therapeutic and prophylactic

141. Hansel, F. K.: Penicillin Sensitivity, Ann. Allergy **7**:619, 1949.

142. Lepper, M. H.; Dowling, H. F.; Robinson, J. A.; Stone, T. E.; Brickhouse, R. L.; Caldwell, E. R., Jr., and Whelton, R. L.: Studies on Hypersensitivity to Penicillin: I. Incidence of Reactions in 1303 Patients, J. Clin. Invest. **28**:826-831, 1949.

143. Feldman, M. D.: Sensitization to Penicillin: The Types of Reactions; Therapy and Prevention, Ohio M. J. **45**:131-135, 1949.

144. Haunz, E. A., and Grinnell, E. L.: Sensitivity Reactions From Penicillin Preparations of Prolonged Action, Ann. Allergy **7**:4-12, 1949.

145. Mallen, M. S., and Cuellar, O.: Immunological Studies with Sera from Penicillin Allergic Patients, Ann. Allergy **7**:1-3, 1949.

146. Cross, W. J.: Oral Reactions to Penicillin, Brit. M. J. **1**:171-173, 1949.

147. Samitz, M. H., and Horvath, P. N.: Observations on Severe Penicillin Reactions, Ann. Allergy **7**:490-491, 1949.

148. Waldbott, G. L.: Anaphylactic Death from Penicillin, J. A. M. A. **139**:526-527 (Feb. 19) 1949.

149. Garai, F.: Successful Densensitization to Penicillin, J. A. M. A. **141**:25-26 (Sept. 3) 1949.

150. Simon, S. W.: Skin Sensitivity to Streptomycin, J. Allergy **20**:56-61, 1949.

measures. Frequent contact with streptomycin over several weeks seems to be responsible in these cases. A method of dry patch testing for sensitivity to streptomycin and dihydrostreptomycin is described (Simon [151]).

Lynn [152] gives a long list of eye disturbances occurring in conjunction with sulfonamide therapy. Harmful effects on the mouth, nose, throat and ear are considered as rare. Typical febrile episodes are described which are usually characterized by a recession of symptoms of the original disease and the development of symptoms suggestive of hypersensitivity. Lynn feels that the allergic nature of sulfonamide reaction has been repeatedly demonstrated.

Among various cases of different reactions to drugs reported are a case of cerebral edema in a 26 year old nurse with atopy (Jenkins [153]); a case of fatal pancytopenia following administration of mesantoin® (methylphenylethyl hydantoin) (Weller and Metcalf [154]); violent tibial pains, chills, fever and an urticarial rash in a highly sensitive patient following administration of phenolphthalein dye (Alvarez [155]), and a case of edema of the uvula following administration of scopolamine (Mayer [156]).

Mitchell, R. W. Vilter and C. F. Vilter [157] report a severe anaphylactoid reaction in a 35 year old woman following the intravenous administration of folic acid. The patient had a history of sensitivity to many common drugs.

Roth, Richards and Shepperd [158] believe that cytochrome C is potentially antigenic and recommend skin testing before its intravenous administration.

Coppinger and Goldner [159] describe a case of fatal anaphylactic shock following the administration of amigen,® a protein hydrolysate.

A case of asthma in which the cause was traced to chlorinated water is discussed by Sheldon and Lovell,[160] who emphasize that chlorination of water may produce sensitivities. The possibility of a hapten mechanism is pointed out.

Bernton, Coulson and Stevens [161] studied two patients with positive skin reactions to water-soluble fractions from cottonseed to determine their sensitivity to cottonseed oil. One patient maintained that cottonseed oil never provoked any reaction; the other claimed that it precipitated gastrointestinal symptoms, a sus-

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151. Simon, S. W.: Dry Patch Tests For Streptomycin Sensitivity, J. Allergy **20**:449-452, 1949.

152. Lynn, J. M.: Sulfonamide Toxicity, California Med. **70**:48-56, 1949.

153. Jenkins, C. M.: "Cerebral Edema" Due to Phenobarbital Sensitivity: Clinical Study of a Case, Ann. Allergy **7**:346-349, 1949.

154. Weller, R. W., and Metcalf, J.: Fatal Pancytopenia Following the Use of Mesantoin, New England J. Med. **241**:17, 1949.

155. Alvarez, W. C.: Violent Reaction to Phenolphthalein, California Med. **71**:38, 1949.

156. Mayer, E. C., Jr.: Edema of the Uvula, a Manifestation of Scopolamine Sensitivity, California Med. **71**:146-147, 1949.

157. Mitchell, D. C.; Vilter, R. W., and Vilter, C. F.: Hypersensitivity to Folic Acid, Ann. Int. Med. **31**:1102-1105, 1949.

158. Roth, L. W.; Richards, R. K., and Shepperd, I. M.: Potential Antigenicity of Parenterally Administered Cytochrome C, Proc. Soc. Exper. Biol. & Med. **70**:116-118, 1949.

159. Coppinger, W. R., and Goldner, M. G.: Fatal Anaphylactic Shock Following the Administration of a Protein Digest (Amigen), J. Allergy **20**:369-374, 1949.

160. Sheldon, J. M., and Lovell, R. G.: Asthma Due to Halogens, Am. Pract. **4**:43-44, 1949.

161. Bernton, H. S.; Coulson, E. J., and Stevens, H.: On Allergy to Cottonseed Oil, J. A. M. A. **140**:869-871 (July 9) 1949.

picion that was not confirmed. It is suggested that specific sensitivity to water-soluble extracts of defatted cottonseed does not imply clinical sensitivity to cottonseed oil. Very similar conclusions in regard to edible vegetable oils were also arrived at by Figley [162]

Corn sugar has been regarded as an extremely important allergen by Randolph and Yeager,[163] who emphasize the widespread use of corn in foods.

A case of asthma in a cabinetmaker who proved to be sensitive to the dusts of kejaat, western cedar and Congo hardwood is reported by Ordman.[164] This patient was promptly relieved by desensitization with combined wood extracts and was kept symptom free by monthly injections.

Brown [165] describes a case of persistent cough and bronchospasm due to exposure to fumes of range oil. Lima and Rocha [166] found 35 positive reactions to tobacco extract in a group of 200 allergic children. In 200 nonallergic children there were 15 positive reactions. Reagins were demonstrated in 15 of the first group and in six of the second group. The incidence of positive reactions proved to be higher in children of mothers using tobacco during gestation.

According to Dees,[167] wheals from allergy and histamine tests tend to be increased after the ingestion of alcohol. She states that the means by which alcoholic beverages can act to intensify allergic reactions are easier to explain than the means whereby they can decrease them.

Death from skin tests in a 57 year old asthmatic woman (subjected to a large series of intracutaneous tests) is reported by Blanton and Sutphin.[168]

The role of humidity in allergic reactions has been investigated by Fraenkel,[169] and a study of emotional factors in allergy has been submitted by Cohen and Abram,[170] who conclude that the initiation of allergic attacks by emotional disturbances is more frequent in women than in men, especially between the ages of 20 and 40. The need for recognition and management of the emotional component in allergic patients is emphasized.

ANTIHISTAMINE DRUGS

Antihistamine drugs are still one of the chief subjects of investigation in the field of allergy. A considerable volume of work regarding their pharmacology and

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162. Figley, K. D.: Sensitivity to Edible Vegetable Oils, J. Allergy **20**:198-206, 1949.

163. Randolph, T. G., and Yeager, L. B.: Corn Sugar as an Allergen, Ann. Allergy **7**:651-661, 1949.

164. Ordman, D.: Bronchial Asthma Caused by the Inhalation of Wood Dust, Ann. Allergy **7**:492-496, 1949.

165. Brown, E. A.: Persistent Cough and Bronchospasm Due to Exposure to Fumes from Range Oil, Ann. Allergy **7**:756-760, 1949.

166. Lima, A. O., and Rocha, G.: Cutaneous Reaction to Tobacco Antigen in Allergic and Non-Allergic Children, Ann. Allergy **7**:528-530, 1949.

167. Dees, S. C.: An Experimental Study of the Effects of Alcohol and Alcoholic Beverages on Allergic Reactions, Ann. Allergy **7**:185-194, 1949.

168. Blanton, W. B., and Sutphin, A. K.: Death During Skin Testing, Am. J. M. Sc. **217**:169-173, 1949.

169. Von Fraenkel, P. H.: Humidity and Allergy: Observations in 150 Cases, U. S. Nav. M. Bull. **49**:280-288, 1949.

170. Cohen, M. B., and Abram, L. E.: A Statistical Study of the Emotional Component in Allergy: Its Relationship to the Age and Sex Distribution of 5583 Patients, J. Allergy **20**:207-210, 1949.

therapeutic use has appeared during the past year. Additional information is also accumulating concerning a number of the newer compounds.

Lehman and Stefko [171] have reported striking results in reducing histamine-induced gastric secretion in dogs and gastric ulcer formation in rats with thephorin® ([2-methyl-9-phenyl-2, 3, 4, 9-]tetrahydro-1-pyridindenehydrogen tartrate). Their results are additional presumptive evidence of the antagonistic action of antihistaminics to histamine.

Benacerraf and Fischel [172] found that when promethazine was given intramuscularly to rabbits in doses of 25 to 100 mg. per kilogram body weight, the larger doses reduced the severity of the Arthus reaction induced by egg albumin. Three doses of 75 mg. per kilogram body weight at four hour intervals prevented reactions to large skin test doses of Streptococcus erythrogenic toxin. It was felt that promethazine decreased capillary damage and permeability.

The effects of tripelennamine and atropine on peptone shock in dogs were compared by Davis and Haterius.[173] Dogs were prepared 10 minutes prior to administration of the drugs. Six controls all died, while five of six given atropine survived. Ten dogs given either tripelennamine or tripelennamine and atropine survived. Davis and Haterius believe that tripelennamine gives better protection than does atropine.

Abramson and Grosberg [174] found that epinephrine introduced into the skin by electrophoresis was 1,000 times as effective as tripelennamine against the effects of histamine introduced later. The reappearance of the epinephrine blanching effect up to five hours after the administration of histamine was found consistent with the prolonged effect of epinephrine in aerosol therapy of the lungs.

Roberts, Crockett and Laipply [175] were unable to prevent the development of experimental anaphylactic hypertensive cardiac lesions in rabbits with diphenhydramine and salicylates, and Winter [176] found that promethazine would not protect rats or guinea pigs against pulmonary edema from injected ammonium chloride.

Lovejoy, Feinberg and Canterbury [177] described a method of bioassay of antihistaminic drugs involving the local inhibition of histamine flare in human subjects. Tripelennamine was used as a standard. They feel that results from this method

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171. Lehman, G., and Stefko, P. L.: The Action of Thephorin upon Histamine Induced Gastric Secretion in Dogs and on Gastric Ulcer Formation in Rats, J. Lab. & Clin. Med. **34**:372-379, 1949.

172. Benacerraf, B., and Fischel, E. E.: Effect of Phenergan (N-Dimethylamino-2-Propyl-1-Thiodiphenylamine, 3277 R. P.) on the Arthus Reaction in Rabbits, Proc. Soc. Exper. Biol. & Med. **71**:349-351, 1949.

173. Davis, J., and Haterius, H.: Comparison of Atropine and Tripelennanine in Treatment of Peptone Shock in Dogs, Proc. Soc. Exper. Biol. & Med. **70**:275-279, 1949.

174. Abramson, H. A., and Grosberg, S.: Skin Reactions: XVI. Comparison of Antihistaminic Action of Pyribenzamine and Epinephrine Introduced into Human Skin by Electrophoresis, Ann. Allergy **7**:325-328, 1949.

175. Roberts, R. C.; Crockett, K. A., and Laipply, T. C.: Effects of Salicylates and Benadryl on Experimental Anaphylactic Hypersensitive Vascular and Cardiac Lesions, Arch. Int. Med. **83**:48-66 (Jan.) 1949.

176. Winter, C. A.: Failure of Antihistaminic Drug "Phenergan" to Protect Against Acute Pulmonary Edema, Proc. Soc. Exper. Biol. & Med. **72**:122-124, 1949.

177. Lovejoy, H. B.; Feinberg, S. M., and Canterbury, E. A.: Local Inhibition of Histamine Flare in Man: A Method of Bioassay of Antihistamine Drugs, J. Allergy **20**:350-357, 1949.

compare well with therapeutic results but point out that its reliability can be proved only by more extensive comparison with clinical findings.

The capacity of antihistaminics to alter the wheal produced in scratch test with ragweed in sensitive patients is another method of comparison used by Schwartz and Wolff.[178] They found that a series of drugs could be arranged in three groups according to their antihistaminic properties. Pyranisamine (neo-antergan®), methapyrilene (histadyl® [01013]), tripelennamine and antazoline were more effective than was diphenhydramine, which, in turn, was more effective than were thonzylamine (neohetramine®) and thephorin.® The ability of the drugs to alter allergic wheals was found to run in about the same order. Differences between members of a particular group were not considered significant.

Loveless and Dworin [179] have reviewed the literature on 11 antihistaminics and conclude on the basis of 13,000 reported trials that tripelennamine, prophenpyridamine and thephorin® are the most satisfactory in a variety of clinical conditions.

Harris [180] has compared the effectiveness of methapyrilene, tripelennamine, diphenhydramine, hydryllin® (a mixture of diphenhydramine and aminophylline) and compound 1695 (xanthine salt of 10-[β-dimethylaminoethyl] phenothiazine) in a wide variety of allergic conditions. He feels that methapyrilene and tripelennamine are a little more useful than diphenhydramine. In bronchial asthma with pollinosis (the only condition under which asthma was benefited at all) hydryllin® seemed the most effective. Compound 1695 proved definitely less effective than the others.

Still another comparative study was reported by A. S. Friedlaender and S. Friedlaender.[181] The clinical and experimental efficiency of diphenhydramine, tripelennamine, antazoline, pyrilamine, thonzylamine and methapyrilene (thenylene®) were compared. As a protective agent against fatal histamine shock in guinea pigs, pyrilamine was most effective and antazoline the least. In whealing experiments on human subjects pyranisamine was also most effective and again antazoline was the least. Somewhat similar results followed the various clinical studies, but the results are described as being much less definite.

Kugelmass [182] has studied the use of diphenhydramine, methapenilene (diatrin®) and tripelennamine in children. He found that gastrointestinal allergies could not be completely avoided without elimination of the responsible allergen. Mild hay fever could be completely controlled, but in severe hay fever specific desensitization was also required. Vasomotor rhinitis was not relieved by antihistaminics alone, and in asthma these drugs proved of value in the primary hereditary type and perhaps in the secondary acquired type but not in the residual long-injury type. Dosages are discussed, and in general methapenilene is given to infants in doses of 5 to 25 mg., children 25 to 75 mg. and adolescents 75 to 200 mg. Somewhat larger doses are required for diphenhydramine and tripelennamine.

178. Schwartz, E., and Wolff, J.: Histamine Antagonists, J. Allergy **20**:32-49, 1949.

179. Loveless, M. H., and Dworin, M.: Allergy and Antihistamine Therapy: A Review, Bull. N. Y. Acad. Med. **25**:473-487, 1949.

180. Harris, H. L.: Therapeutic Effects of Certain Antihistamine Drugs in Allergic Conditions: Comparative Study, Ann. Allergy **7**:206-214, 1949.

181. Friedlaender, A. S., and Friedlaender, S.: Correlation of Experimental Data with Clinical Behavior of Synthetic Antihistaminic Drugs, Ann. Allergy **7**:83-90, 1949.

182. Kugelmass, I. N.: Antihistaminic Therapy of Allergic Disorders in Infants and Children, New York J. Med. **49**:2313-2318, 1949.

McGavack [183] discusses the clinical use of diphenhydramine and points out that in this drug a mild scopolamine-like action changes its value, making it useful as a mild sedative. In general 150 mg. is recommended as an initial daily dose to be increased if necessary. Results in a variety of clinical conditions are presented.

Zolov [184] has treated 26 patients with small intravenous doses of diphenhydramine and found the incidence of side reactions to be low. His clinical results were not materially different from those usually reported. Of 14 patients with asthma three had excellent results, five were improved and six derived no benefit. Excellent results were reported in one case of ivy poisoning, in two of four cases of hay fever and in one of two cases of neurodermatitis. Of three cases of vasomotor rhinitis two were improved, but there were no excellent results.

Lee [185] obtained no result with diphenhydramine in a 25 year old man with histamine headache. This patient was relieved by desensitization with histamine.

In a case of cold hypersensitivity Rothschild [186] found that the effects on blood pressure, gastric secretion and the local tissues were reversed by diphenhydramine. He feels that this finding supports the view that histamine release is responsible for this condition.

Feinberg and Bernstein [187] treated 51 asthmatic patients with 2 per cent tripelennamine in aerosol form. Most of these patients were not responsive to oral administration of the drug, but 10 obtained effective relief and 13 slight relief from the aerosol.

MacQuiddy [188] reported 150 selected cases treated with doxylamine (decapryn®) succinate. In this series 50 mg. doses were originally used, but this dose was later cut to 25 mg. and then to 12.5 mg. by day and 25 mg. at bedtime. These smaller doses proved effective and materially reduced the incidence of side reactions. The cases are grouped according to age, sex and the condition or combination of conditions treated.

Schwartz and Leibowitz [189] have found thephorin® to be an effective drug of low toxicity. They report symptomatic relief in 46 of 60 patients with hay fever, 33 of 55 with vasomotor rhinitis and 3 of 10 with asthma. No case of vernal catarrh was benefited. In children treated, Levin and Moss [190] obtained relief in 81 per cent of those with hay fever, 75 per cent with pollen asthma, 73 per cent with perennial asthma, 66 per cent with allergic rhinitis and 75 per cent with infantile eczema and urticaria. Their report covers 109 cases, in 20 per cent of which there were side reactions. Only 8 per cent of the reactions were severe enough to warrant dis-

183. McGavack, T. H.: The Nature of Benadryl Activity and Its Clinical Applications, Ann. Allergy **7**:232-238, 1949.

184. Zolov, B.: Benadryl: Intravenous Use in Allergy, Ann. Allergy **7**:254-257, 1949.

185. Lee, J. H., Jr.: Use of Benadryl in Histamine Headache, U. S. Nav. M. Bull. **49**:94-96, 1949.

186. Rothschild, J. L.: Effects of Benadryl on Systemic Manifestations of Cold Hypersensitivity, J. Allergy **20**:62-65, 1949.

187. Feinberg, S. M., and Bernstein, T. B.: Nebulized Pyribenzamine in Nasal and Bronchial Allergy, J. Lab. & Clin. Med. **34**:1078-1080, 1949.

188. MacQuiddy, E. L.: The Clinical Application of Antihistamine Drugs, Nebraska M. J. **34**:123-124, 1949.

189. Schwartz, E., and Leibowitz, H.: Thephorin: A New Histamine Antagonist in the Symptomatic Treatment of Allergy, New York J. Med. **49**:533-534, 1949.

190. Levin, S. J., and Moss, S. S.: Thephorin: Clinical Results in Allergic Children, J. Pediat. **34**:616-620, 1949.

continuing the drug. It is pointed out that thephorin® in children is a mild sedative in contrast to its stimulating action in adults.

Criep and Aaron [191] have found that thonzylamine compares favorably with other antihistaminics, both in children and in adults. They have encountered fewer side reactions with this than with other drugs and consider it safer.

Halpern [192] and Shulman [193] have used promethazine (*3277* RP) clinically. Halpern found it of value in serum sickness, urticaria, angioneurotic edema, hay fever and allergic purpura. It was less effective in asthma, migraine and pruritus. Shulman obtained marked improvement in seven of 10 cases of asthma, two of four of eczema, three of nine of contact dermatitis and two of four of migraine. He recommends doses of 6.5 to 25 mg. daily.

Schiller and Lowell [194] report favorable therapeutic responses with prophenpyridamine in 84 patients with hay fever, allergic rhinitis and urticaria. Side reactions, all of them mild, occurred in 10 cases.

Pyrilamine was tried by Schwartz, Levin and Kurtz [195] in 141 allergic patients. Of these, 61.7 per cent experienced relief. Results were best in hay fever, poorest in asthma. Toxic reactions occurred in 35 cases (24.8 per cent).

Saletta [196] obtained moderately good to excellent results in 27 patients (except one asthmatic patient) treated with methapyrilene. In ragweed hay fever excellent results were obtained only in patients under desensitization treatment.

Another new antihistaminic, chlorocyclizine (perazil®), is discussed by Jaros and Castillo.[197] This compound in 100 mg. doses showed marked ability to inhibit the histamine whealing response for 24 hours It gave a low incidence of toxic side effects. The prolonged effect was also apparent on clinical trials. In 50 mg. doses it seemed to have a higher efficiency and a lower rate of toxicity than tripelennamine. Excellent results were obtained in 22 of 23 patients with hay fever, 18 of 21 with vasomotor rhinitis, two with allergic sinusitis and two of 13 with asthma. Side reactions occurred in 48 per cent of 84 cases.

Two other drugs, β-(paramethylbenzhydryloxy)-N,N-dimethylethylamine hydrochloride reported by Shulman and Fuchs [198] and compound 194-B (N,N-

191. Criep, L. H., and Aaron, T.: Antihistaminic Drugs in Pediatric Allergy, J. Pediat. **34**:414-420, 1949.

192. Halpern, B. N.: Recent Advances in the Domain of the Antihistaminic Substances: The Phenothiazine Derivatives, Bull. New York Acad. Med. **25**:323-330, 1949.

193. Shulman, M. H.: Phenergan (R. P. 3277) Preliminary Report of Clinical Effectiveness, Ann. Allergy **7**:506-509, 1949.

194. Schiller, I. W., and Lowell, F. C.: Trimeton: A New Antihistaminic Drug; A Clinical Evaluation, New England J. Med. **240**:215-216, 1949.

195. Schwartz, E.; Levin, L., and Kurtz, M.: The Symptomatic Treatment of Allergic Diseases with Neoantergan, New York J. Med. **49**:1059-1060, 1949.

196. Saletta, S. N.: A New Antihistaminic Compound for the Treatment of Urticaria and Hay Fever, Ann. Allergy **7**:366-367, 1949.

197. Jaros, S. H., and Castillo, J. C., and de Beer, E. J.: The Clinical Application of a New Piperazine Compound: I. Human Pharmacology, Ann. Allergy **7**:458-465, 1949. Jaros, S. H.: The Clinical Application of a New Piperazine Compound: II. Clinical Observations, ibid. **7**:466-470, 1949.

198. Schulman, P. M., and Fuchs, A. M.: Clinical Experiences with B-(P-Methyl-Benzhydryloxy)-Ethyldimethylamine Hydrochloride: A New Antihistaminic, Ann. Allergy **7**:502-505, 1949.

dimethyl-N′-2-thiazolyl-N′-p-methoxy-benzyl-ethenediamine) reported by Bernstein and Feinberg [199] are said to be effective clinically.

Hartman [200] discussed delayed action preparations of antihistaminic drugs and their probable uses. The chief indication for such preparations is the prevention of nocturnal distress after the effects of ordinary preparations have worn off.

Churchill and Gammon [201] have found that in patients with petit mal seizures diphenhydramine tended to decrease the spike wave abnormalities. Tripelennamine, on the other hand, tended to increase them, and one patient tested had a grand mal attack. It is suggested that antihistamine drugs must be used with care in the treatment of epileptic patients.

Yonkman and Mohr [202] feel that antihistamine drugs should be of value in epinephrine-fast patients. They believe that in such cases histamine is released when the epinephrine is given and that it counteracts the bronchodilatation.

The toxicity of various antihistaminic drugs has been compared by Schwartz [203] in adjusted therapeutic doses in 781 allergic patients. He found side effects in 61.3 per cent of 217 patients treated with diphenhydramine, 35.7 per cent of 216 treated with tripelennamine, 24.8 per cent of 141 treated with pyranisamine, 22.7 per cent of 91 treated with antazoline, 20 per cent of 89 treated with methapyrilene and 7.25 per cent of 111 treated with thonzylamine.

Cases of fatal poisoning with antihistamine drugs are reported by Davis and Hunt [204] and Rives, Ward and Hicks.[205] The former reported the case of a 2 year old boy who took 474 mg. of diphenhydramine and the latter the case of a 16 month old girl who took 100 mg. of methapyrilene.

Cases of agranulocytosis and urinary obstruction following administration of tripelennamine are reported by Cahan, Meilman and Jacobson [206] and Wolfson.[207]

Leopold [208] has concluded that diphenhydramine has no effect on the hematopoietic system.

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199. Bernstein, T. B., and Feinberg, S. M.: Histamine Antagonists: XIV. An Experimental and Clinical Study of N,N-Dimethyl-N′-2-Thiazolyl-N′-P-Methoxybenzyl-Ethylenediamine Hydrochloride (194-B), J. Lab. & Clin. Med. **34**:1007-1009, 1949.

200. Hartman, M. M.: Possible Uses of a Delayed Action Antihistaminic, Ann. Allergy **7**:679-680, 1949.

201. Churchill, J. A., and Gammon, G. D.: The Effect of Antihistaminic Drugs on Convulsive Seizures, J. A. M. A. **141**:18-21 (Sept. 3) 1949.

202. Yonkman, F. F., and Mohr, F. L.: An Approach to the Problem of "Epinephrine Fastness," Ann. Allergy **7**:60-61, 1949.

203. Schwartz, E.: Comparative Toxicity and Side Effects of the Antihistaminic Drugs, Ann. Allergy **7**:770-777, 1949.

204. Davis, J. H., and Hunt, H. H.: Accidental Benadryl Poisoning: Report of a Fatal Case, J. Pediat. **34**:358-361, 1949.

205. Rives, H. F.; Ward, B. B., and Hicks, M. L.: A Fatal Reaction to Methapyrilene (Thenylene®), J. A. M. A. **140**:1022-1024 (July 23) 1949.

206. Cahan, A. M.; Meilman, E., and Jacobson, B. M.: Agranulocytosis Following Pyribenzamine, New England J. Med. **241**:865-867, 1949.

207. Wolfson, S. A.: Urinary Obstruction Due to Tripelennamine Hydrochloride, J. A. M. A. **140**:958 (July 16) 1949.

208. Leopold, H. C.: The Absence of the Effects of Benadryl on the Hematopoietic System, Ann. Allergy **7**:510-512, 1949.

The possibility of withdrawal symptoms developing after treatment with antihistaminic drugs is suggested by Cherry,[209] who reports three cases in which such symptoms occurred.

The indiscriminate use of antihistaminic drugs in the treatment of respiratory allergies has been criticized by Halpin,[210] who points out their limitations, such as their lack of value in perennial allergic rhinitis and asthma. When indications of allergies occur, Halpin still considers diphenhydramine and tripelennamine the drugs of choice. Dintenfass[211] has also written on the limitations of the antihistaminic drugs, indicating their purely palliative action, their unpredictability, the frequency with which side reactions limit their use and the lack of definite knowledge of the role of histamine, and hence of these drugs, in allergy.

Hunter[212] has mentioned the questionable value of antihistaminics in vasomotor rhinitis and their lack of proved value in asthma. He considers them of more definite value in hay fever and suggests that side effects may be minimized by their administration after meals.

The use of the histamine antagonists in the treatment of the common cold has been discussed by a number of physicians (e. g., Brewster,[213] Middleton and Rider,[214] and Arminio and Sweet[215] and Phillips and Fishbein[216]). Their papers will not be further reviewed here.

ACTH

The use of ACTH in allergic diseases has been suggested recently, and a few papers on this subject have appeared during 1949. The effects of ACTH on bronchial asthma have been studied by Randolph and Rollins,[217] Rose,[218] Bordley, Harvey, Howard and Newman[219] and Elkinton and his associates.[220]

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209. Cherry, A.: Antihistamine Withdrawal Symptoms: Report of Three Cases, M. J. Australia **2**:540, 1949.

210. Halpin, L. J.: An Appraisal of Therapeutic Procedures in Respiratory Allergy, South. M. J. **42**:115-118, 1949.

211. Dintenfass, A.: An Evaluation of the Antihistaminic Drugs, J. M. Soc. New Jersey **46**:66-68, 1949.

212. Hunter, R. B.: The Experimental and Clinical Use of Antihistamine Drugs, Edinburgh M. J. **56**:54-61, 1949.

213. Brewster, J. M.: Antihistaminic Drugs in the Therapy of the Common Cold, U. S. Nav. M. Bull. **49**:1-11, 1949; Treatment of Common Colds with an Antihistaminic Drug, Illinois M. J. **96**:302-306, 1949.

214. Middleton, J. W., and Rider, J. A.: Antihistaminics in the Treatment of the Common Cold: A Preliminary Report, Dis. Chest **16**:885-903, 1949.

215. Arminio, J. J., and Sweet, C. C.: The Prophylaxis and Treatment of the Common Cold with Neohetramine (Thonzylamine Hydrochloride), Indust. Med. **18**:509-511, 1949.

216. Phillips, W. F. P., and Fishbein, W. I.: An Antihistaminic Analgesic Preparation in the Therapy of Colds: A Preliminary Report, Indust. Med. **18**:526, 1949.

217. Randolph, T. G., and Rollins, J. P.: Relief of Allergic Diseases by ACTH Therapy, in Mote, J. R.: Proceedings of the First Chemical ACTH Conference, Philadelphia, The Blakiston Company, 1950, pp. 479-490.

218. Rose, B.: Studies on the Effect of ACTH on Eosinophilia and Bronchial Asthma, in Mote, J. R.: Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950, pp. 491-504.

219. Bordley, J. E.; Harvey, A. M.; Howard, J. E., and Newman, E. V.: Preliminary Report on the Use of ACTH in the Hypersensitive State, in Mote, J. R.: Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950, pp. 469-478.

220. Elkinton, J. R.; Hunt, A. D., Jr.; Godfrey, L.; McCrory, W.; Rogerson, A., and Stokes, J., Jr.: Effects of ACTH in Patients with Collagen and Allied Diseases, in Mote, J. R.: Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950, pp. 429-436.

Randolph and Rollins treated three patients with severe asthma (one with evidence of emphysema) with ACTH, using 25 mg. doses intramuscularly every six hours. This dosage was maintained for two days in two patients and for three days in the third. Clinical improvement was noted in all three patients in four to five hours. It was accompanied with increased vital capacity and a fall in the eosinophil count. After treatment the patients remained symptom free for about 21 days, after which time symptoms began to recur. At the end of four weeks they were rehospitalized with symptoms of former severity, which subsided again under a second course of treatment with ACTH. A fourth patient with intermittent asthma obtained only 50 per cent relief with ACTH.

Rose [218] studied six patients with asthma treated with ACTH under carefully controlled conditions. These patients, after preliminary studies, were given divided daily doses of 100 to 150 mg. of ACTH which were lowered on subsequent days, a total of 475 to 500 mg. being given. The symptoms began to disappear in 24 to 36 hours. Four of the patients had complete remissions in 48 hours. The other two did not have complete remissions. The longest remission recorded was one month, following which the symptoms returned over a two week period. Positive results of skin tests in three of these patients were not altered by administration of ACTH.

Bordley and his associates [219] report seven patients with severe chronic asthma, all of whom were symptom free after two to seven days of ACTH therapy. These patients received 40 to 100 mg. of ACTH a day with a gradual lowering of the dose to 20 mg. Treatment was continued for from nine to 20 days.

A patient with status asthmaticus who obtained complete relief with three courses of ACTH is reported by Elkinton and his associates.[220]

Rose [218] treated a case of Loeffler's syndrome and a case of tropical eosinophilia with ACTH. In both instances there was a marked rapid fall in the number of eosinophils. The patient with Loeffler's syndrome obtained a remission after the ACTH therapy. The patient with tropical eosinophilia recovered with oxophenarsine (mapharsen®) therapy.

Randolph and Rollins [217] report four patients with hay fever treated with 25 mg. doses of ACTH every six hours. Treatment was continued for 24 hours in one case, for 48 hours in two and for 56 hours in one. All patients noted marked improvement of symptoms within the first hour, and only one had a mild recurrence of hay fever during that season.

Randolph and Rollins have also studied results of ACTH in atopic dermatitis and have found that the symptoms are relieved on treatment but tend to recur with increased severity afterward. A number of patients with food allergies were able to eat the foods to which they were sensitive without symptoms developing while receiving treatment with ACTH.

Favorable results in the treatment of disseminated lupus erythematosus have been reported by Bordley and his associates [219] and Elkinton and his associates.[220] Elkinton has also treated two patients with acute rheumatoid arthritis with ACTH and obtained rapid remissions of symptoms, which promptly returned when treatment was stopped. One of these patients was relieved with daily doses of 40 mg. but later required up to 75 mg. to maintain the remission. Treatment in this patient was discontinued after 148 days when symptoms suggestive of Cushing's syndrome appeared.

Bordley and his associates [219] treated two patients with severe serum disease type of reaction with penicillin, using 100 mg. of ACTH in divided doses for two days and then rapidly lowering the dose to 20 mg. a day. One patient was relieved of symptoms within 18 hours and the other within 36 hours.

A patient with periarteritis nodosa treated with 10 mg. of ACTH every six hours is described by Goldman and his associates.[221] This patient showed marked improvement while under treatment but relapsed a few days after therapy was discontinued.

BASIC STUDIES

Fitzgerald and Sherman,[222] working with pollen extracts of timothy, June and orchard grass, found that in grass-sensitive patients with hay fever symptoms adequate clinical protection developed when they were treated with any of the grasses. It was further shown that in seven of 12 cases blocking antibody could be demonstrated against all three grasses, regardless of which one had been administered. Normal persons given massive doses of grass pollen extracts developed blocking antibodies against related grasses as well as against the one used experimentally. The results of skin tests in such persons remained negative. Fitzgerald and Sherman believe that their findings indicate a close relation between the different grass pollen antigens.

Criep and Levine [223] have studied both allergic and nonallergic patients with a dermofluorometer (consisting of an ultraviolet light source and a photoelectric cell by means of which fluorescence can be detected and plotted) and administration of fluorescein intravenously. The degree of fluorescence gives a measure of circulation time and capillary permeability. Fluorescence was studied over normal skin and over wheals induced by histamine, ragweed extract and isotonic sodium chloride solution as well as over urticarial wheals and following the administration of tripelennamine and epinephrine. It was found that fluorescence curves in allergic patients fell within normal limits. Histamine wheals in normal and allergic persons showed the same degree of hyperfluorescence, which was reduced by epinephrine. It was further found that neither epinephrine nor tripelennamine affected the curves for normal skin and that massive doses of tripelennamine orally seemed to reduce fluorescence in histamine wheals.

Adams [224] has developed a nutritional schedule consisting of a protein hydrolysate, a source of vitamin B complex (derived from liver concentrate, rice polishings, dried yeast, wheat germ and unprocessed honey) and an oil-in-water emulsion of all other vitamins, which he feels is an adequate source of all vitamins and essential amino acids and polypeptides. He feels that this schedule shows promise in certain cases of eczema and asthma.

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221. Goldman, R.; Adams, W. S.; Beck, W. S.; Levin, M.; Bassett, S. H., and White, A.: The Effect of ACTH on 1 Case of Periarteritis Nodosa, in Mote, J. R.: Proceedings of the First Clinical ACTH Conference, Philadelphia, The Blakiston Company, 1950, pp. 437-446.

222. Fitzgerald, J. D. L., and Sherman, W. B.: The Specificity of Blocking Antibody Induced by Grass Pollen Extracts, J. Allergy **20**:286-291, 1949.

223. Criep, L. H., and Levine, M. I.: Studies of Capillary Permeability in Allergy with the Dermofluorometer, J. Allergy **20**:185-197, 1949.

224. Adams, T. J.: Protein and Vitamin Metabolism in the Allergic State, Ann. Allergy **7**:482-489, 1949.

Dalton [225] believes that the eosinophil leukocyte is a part of the mechanism of the allergic response rather than a result thereof and suggests that it may be involved in the release of histamine. He points out that allergic reactions tend to occur at the site of eosinophilic concentration, that allergic responses elsewhere are accompanied with local or general eosinophilia or both and that eosinophilia and allergy induced experimentally develop after the same period of time.

Orban [226] has investigated 200 patients for eosinophilia and concluded that a standard of 400 eosinophils per cubic millimeter of blood is of value in the diagnosis of allergy.

Pulmonary absorption of penicillin has been studied by Gaensler, Beakey and Segal,[227] who administered the drug intratracheally to normal volunteers. They found that on intratracheal administration the penicillin was readily absorbed into the blood stream, although the high levels attained by parenteral administration were not reached. On the other hand, therapeutic levels were maintained twice as long. Administration of penicillin as an aerosol led to the high levels of parenteral administration, but therapeutic levels were maintained for only one-third as long. It is suggested that intratracheal administration of penicillin may be a practical procedure under some circumstances. In another paper [228] various diluents for the intratracheal administration of penicillin are compared and discussed.

The absorption of an aerosol of phenolsulfonphthalein from the lung as indicated by its rate of urinary excretion was studied by Abramson and his associates.[229] These authors believe that absorption is through the lung and that the gastrointestinal tract and upper respiratory tract play only a minor part. From these studies they conclude that present techniques of aerosol therapy present many more variables than are desirable. A method of determining the rate of delivery by the nebulizer is presented in another communication.[230]

MISCELLANEOUS ALLERGIES

The role of allergy in periarteritis nodosa is discussed by Harris and Laws,[231] who feel that a basic allergic reaction is involved in many cases. Hejtmancik, Schofield and Herrmann [232] present two cases of this disease under the title "Allergic Cardiovascular Disease."

Gelfand and Aronoff [233] reviewed the records at Bellevue Hospital and found that only four cases of periarteritis nodosa were diagnosed ante mortem between

225. Dalton, D. J.: The Eosinophile Leukocyte: Eosinophilia and Allergy, Lancet **2**:607-609, 1949.

226. Orban, T. D.: Eosinophilia in Allergy, M. J. Australia **1**:678-679, 1949.

227. Gaensler, E. A.; Beakey, J. F., and Segal, M. S.: Pharmacodynamics of Pulmonary Absorption in Man: I. Aerosol and Intratracheal Penicillin, Ann. Int. Med. **31**:582-594, 1949.

228. Beakey, J. F.; Gaensler, E. A., and Segal, M. S.: Pharmacodynamics of Pulmonary Absorption in Man: II. The Influence of Various Diluents on Aerosol and Intratracheal Penicillin, Ann. Int. Med. **31**:805-820, 1949.

229. Abramson, H. A.; Reiter, C.; Gettner, H. H., and Sklarofsky, B.: Aerosols: I. The Urinary Excretion of Inhaled Phenolsulfonphthalein Mists, Ann. Allergy **7**:761-769, 1949.

230. Abramson, H. A.; Sklarofsky, B., and Reiter, C.: Procedure for Determination of Aerosol Delivery and Stability During Nebulization, Ann. Allergy **7**:612-618, 1949.

231. Harris, J. F., and Laws, C. L.: Periarteritis Nodosa, Ann. Allergy **7**:105-107, 1949.

232. Hejtmancik, M. R.; Schofield, N. D., and Herrmann, G. R.: Allergic Cardiovascular Disease with Report of 2 Cases of Periarteritis Nodosa, Am. J. M. Sc. **217**:187-193, 1949.

233. Gelfand, M. L., and Aronoff, S.: Periarteritis Nodosa—Possible Relation to the Increased Usage of Sulfonamides, Ann. Int. Med. **30**:919-924, 1949.

1916 and 1937, while 14 cases were recognized between 1937 and 1946. A history of bronchial asthma was obtained in 57 per cent of these 14 patients and eosinophilia of 10 per cent or more was found in 43 per cent of them. Gel and Arnoff feel that hypersensitivity to the sulfonamide drugs as an etiological factor may be suggested by the above findings.

On the other hand, Wold and Barker [234] reviewed the records of 30 cases diagnosed at autopsy and found that a history or evidence of any allergic reaction or drug sensitivity was infrequent.

Rockwell [235] suspects allergy of playing a role in rheumatoid arthritis and feels that clinical results following the intravenous administration of histamine together with bacterial desensitization and elimination of offending foods have been encouraging.

Criep [236] discusses a group of collagenous diseases including serum disease, lupus erythematosus, Libman-Sacks syndrome, scleroderma, rheumatic fever, periarteritis nodosa, dermatomyositis, nephrosclerosis, sclerema neonatorum, and thromboangiitis obliterans. He believes that both clinical and experimental evidence indicate that "the development of some of these conditions may be closely related to the phenomena of hypersensitiveness."

Criep and Mayer [237] have confirmed previous observations that large doses of horse serum may produce lesions like those of periarteritis nodosa and rheumatic cardites in experimental animals.

Tocker [238] describes a case of Loeffler's syndrome in a patient with asthma and ragweed pollinosis. He believes the condition is a phase of an allergic pulmonary reaction rather than a distinct entity. Of 36 reported cases of Loeffler's syndrome reviewed in the literature, 69 per cent had a history of asthma.

Falk and Newcomer [239] encountered Loeffler's syndrome in two patients under treatment for syphilis with penicillin in oil and wax. Eosinophilic counts showed 44 per cent eosinophils in one of these patients and 37 per cent in the other. The wax was suspected but was not definitely proved to be the cause.

A case of pneumonia associated with pericardial effusion and venous thrombosis is reported by Dickie and Grimm.[240] This patient had a history of bronchial asthma. Further indication of hypersensitivity was furnished by blood eosinophilia and eosinophils in the sputum and pericardial fluid. Another case with an eosinophilic pericarditis and pleural effusion is reported by Zivitz and Oshlay.[241]

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234. Wold, L. E., and Barker, N. W.: Periarteritis Nodosa (Essential Polyarteritis), Minnesota Med. **32**:715-720, 1949.

235. Rockwell, G. E.: The Role of Allergy in Rheumatoid Arthritis and a Suggested Treatment, Ann. Allergy **7**:195-198, 1949.

236. Criep, L. H.: Collagen Disease: Its Relation to Hypersensitiveness, J. Allergy **20**:116-132, 1949.

237. Criep, L. H., and Mayer, L. D.: Experimental Collagen Disease from Hypersensitization to Streptococcus Toxin, J. Allergy **20**:243-253, 1949.

238. Tocker, A. M.: Transitory Pulmonary Infiltrations (Loeffler's Syndrome) with a Case Report, J. Allergy **20**:211-221, 1949.

239. Falk, M. S., and Newcomer, V. D.: Loeffler's Syndrome: Occurrence in 2 Patients Treated with Penicillin in Oil and Wax, J. A. M. A. **141**:21-22 (Sept. 3) 1949.

240. Dickie, H. A., and Grimm, E.: Loeffler's Syndrome with Associated Eosinophilic Polyserositis, Am. J. Med. **7**:690-693, 1949.

241. Zivitz, N., and Oshlay, J. A.: Eosinophilic Pleural Effusion and Pericarditis with Effusion in an Allergic Subject, J. Allergy **20**:136-143, 1949.

Fox and Livingston [242] have discussed the role of allergy in the common cold in considerable detail.

GENERAL REVIEWS

Cohen and Abram [243] present a series of cases illustrating reasons for failure in the management of patients with allergies. The series includes mistakes in diagnosis, incomplete diagnosis and inadequate treatment.

Glaser [244] discusses the problems of allergy in pediatric practice. Their relation to general practice is reviewed by Clark,[245] Cooke [246] and Wolf.[247]

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242. Fox, N., and Livingston, G.: Role of Allergy in the Epidemiology of the Common Cold, Arch. Otolaryng. **49**:575-586 (June) 1949.

243. Cohen, M. B., and Abram, L. E.: Cases Illustrating Some Causes for Failure in the Management of Patients with Allergy, Ohio M. J. **45**:561-564, 1949.

244. Glaser, J.: Pediatric Allergy, Ann. Allergy **7**:268-294, 1949.

245. Clark, M. S.: Allergy in General Practice, North Carolina M. J. **10**:580-584, 1949.

246. Cooke, R. H.: The Allergy Factor in Disease, Ann. Int. Med. **31**:17-32, 1949.

247. Wolf, A. F.: The Status of Allergy in Relation to Medical Practice, South. M. J. **42**:808-812, 1949.

Abstracts from Current Literature

Ear

HAEMOSTASIS IN THE FENESTRATION OPERATION. I. SIMSON HALL and A. MCCALLUM MILLAR, J. Laryng. & Otol. **64**:233 (May) 1950.

The desirability of hemostasis in fenestration surgery is discussed. Hall and McCallum believe that by lowering the blood pressure hemostasis might be accomplished. They found that the blood pressure could be lowered by using a high spinal anesthesia in addition to this pentothal sodium intravenously and oxygen intratracheally. They consider the optimum level to be a systolic pressure of 70 to 80 mm. Hg.

The procedure used by the authors consists of premedication with ⅓ grain (20 mg.) of pantopon (a mixture of opium alkaloids) and 1/150 grain (0.40 mg.) of scopolamine hydrobromide given one hour preoperatively, anesthesia induced by the intravenous administration of this pentothal sodium, intubation and administration of oxygen. An intrathecal injection of 1.5 to 2 cc. of heavy dibucaine hydrochloride (nupercaine®) is then made into the second lumbar interspace. When the blood pressure fall was excessive, this was readily corrected by the use of methamphetamine hydrochloride. Such a routine has given the authors excellent hemostasis and good anesthesia.

LEJEUNE AND LEWIS, New Orleans.

THE LIMITS OF IMPROVEMENT OF HEARING FOLLOWING THE FENESTRATION OPERATION. H. DAVIS and T. E. WALSH, Laryngoscope **60**:273 (March) 1950.

A thorough analysis is made of 195 consecutive cases of fenestration operations. Hearing before and shortly after operation (up to four months) is compared.

It is shown that after the best possible fenestration operation there will still be a loss of hearing of at least 20 decibels and that the maximum possible gain is the result of this figure subtracted from the maximum possible loss from conductive deafness (60 decibels), or 40 decibels.

The "surgical deficit," or that amount by which the surgeon fails to achieve the best possible result, is 6 to 7 decibels, but even 12 decibels can be considered reasonable.

Among other things discussed are the surgical failures, means of evaluating the surgeon's skill and the selection of cases.

HITSCHLER, Philadelphia.

OTITIS MEDIA WITH EFFUSION: A CHALLENGE TO OTOLARYNGOLOGY. GORDON D. HOOPLE, Laryngoscope **60**:315 (April) 1950.

Otitis media with effusion is an important otological condition and one that is often missed. In nine of 10 cases there is no fluid level.

The etiology is not clear. Otitis media does not occur in all cases of blocked eustachian tubes. Regional blockage of the lymph drainage and allergy have been mentioned. Psychic, endocrine and cardiac lesions may be factors.

HITSCHLER, Philadelphia.

REPORT OF FOUR HUNDRED AND TWENTY-FIVE FENESTRATION OPERATIONS FOR CLINICAL OTOSCLEROSIS. J. MORRISSET SMITH, South. M. J. **41**:198 (March) 1948.

Smith makes a third report of his surgical experience with the fenestration operation for the relief of deafness. It includes 425 operations covering a period of 7½ years. The anatomy, physiology and pathology of the structures involved are discussed briefly. The indication for the operation is a drop in the air conduction below the practical conversational level in the three important speech frequencies of 512, 1,024 and 2,048, with the bone conduction above the 25

decibel level in the same frequencies. The drum membrane should be intact and the eustachian tube patent, with a complete absence of any middle ear or mastoid infection. The operation is not limited to the true otosclerosis patients. A previous middle ear and mastoid infection is not a contraindication to the operation if the infection has long since subsided and the drum is healed. Operation in the presence of a limited loss of nerve function is not contraindicated; in such cases there is a chance that the progress of the disease will be arrested and practical hearing preserved. The technique of the operation and the postoperative management are discussed in some detail. Audiograms illustrating nine different cases are presented.

Smith's conclusions follow:

"The fenestration operation makes it possible to restore practical and lasting airborne hearing in properly selected cases.

"It is essentially an operation for conduction deafness. There must be sufficient nerve function present for a successful hearing result.

"An accurate test of the bone conduction is the best means of determining the correct indications for the operation.

"The chances of restoring practical hearing decrease in direct proportion to the increase in the loss of nerve function.

"The operation is very complex and difficult and will eventually find its proper place in the hands of a few highly trained, skilled technicians specializing in this work and devoting most of their time to it."

SINGLETON, Dallas, Texas.

CHRONIC SECRETORY OTITIS. WALTER T. HOTCHKISS, South. M. J. **41**:727 (Aug.) 1948.

Hotchkiss states that in the past six years he has seen approximately 30 cases of chronic secretory otitis which in spite of repeated myringotomy have lasted from six months to 3½ years. His discussion is confined to such cases. The symptoms of chronic secretory otitis are the same as those of the acute disease. The patient complains of unilateral or bilateral deafness with intense blocking in one or both ears. He may hear or feel bubbles in the ear. His own voice sounds unduly loud, and in certain positions of the head the symptoms may temporarily disappear. In the presence of a fluid line or of air bubbles the diagnosis is simple. But in many cases the drum membrane is so thickened that discoloration, fluid lines and air bubbles cannot be seen. In such cases the diagnosis can almost always be made by the use of the listening tube and gentle inflation of the ear. In most cases inflation will clearly demonstrate the distinct sounds of fluid in the middle ear. In approximately half the cases a distinct and characteristic type of sound was obtained which is described as the "choked" type of inflation; this sound is heard when gentle constant air pressure is applied through the eustachian catheter and momentarily the flow of air in the middle ear is heard, then apparently abruptly stopped even though air pressure is maintained in the catheter. If the inflation is stopped for a moment and then repeated, the same type of sound is again heard. After the diagnosis has been established, such contributing causes as nasal allergy and nasal, tubal and pharyngeal disease should be diagnosed and properly treated. The use of radium in the nasopharynx is indicated in certain well selected cases. Paracentesis with or without local anesthesia followed by capillary or mass suction for the removal of the fluid is advised in these cases. In persistent cases that fail to respond to the usual procedures, a permanent perforation 2 or 2.5 mm. in diameter may result in a cure. Hotchkiss has resorted to this type of treatment in a few cases of older patients. For making permanent openings, specially designed corneal trephines are used.

SINGLETON, Dallas, Texas.

PSEUDO LABYRINTHINOPATHIES. MARIO RIUS, An. oto-rino-laryng. Uruguay **18**:52, 1948.

Rius discusses a number of conditions which present symptoms of infection of the labyrinth and yet do not present any actual pathological condition in the labyrinth per se. He terms these conditions "pseudolabyrinthinopathies" and divides them into the following groups: (1) patho-

logical conditions of the middle ear such as sero-otitis or catarrhal tubotympanitis, usually associated with acute upper respiratory tract infections or allergic phenomena; inflation of the eustachian tube usually clears up the symptoms; (2) neuritis of the eighth nerve, commonly associated with syphilitic involvement; (3) acoustic tumor, for which careful audiometric and vestibular tests plus a thorough neurological examination should be made in all cases (in the case which Rius has reported many of the symptoms were masked, but careful study later revealed a cerebellopontile tumor); (4) traumatic lesions of the eighth nerve, often associated with a history of traumatism; careful data will establish a true diagnosis; (5) hydrocephalus of the posterior fossa, which very often produces inconclusive symptoms so that an exact diagnosis is difficult and errors in localization may be common; x-ray examination and lumbar punctures plus audiometric, vestibular and neurological examinations may help in a careful evaluation of the disease; (6) syringomyelia, which may produce symptoms of infection of the labyrinth, and (7) cortical lesions involving the vestibular tracts which will produce symptoms of infection of the labyrinth. In conclusion, Rius states that there are many middle ear and intracranial conditions which will produce symptoms lasting days, months and even years. It is very important to recognize these clinical forms so that errors in diagnosis can be avoided, and finally it may be necessary in certain cases to observe the patient for a long period in order to establish an exact diagnosis and avoid an erroneous one based on a single examination.

PERSKY, Philadephia.

EFFECT OF DISCONTINUOUS PENICILLIN THERAPY IN ACUTE SUPPURATIVE OTITIS WITH SPECIAL REFERENCE TO OTITIS IN CHILDREN. TORBEN JERSILD and FLEMMING KIØRBOE, Acta oto-laryng. **38**:8 (Feb.) 1950.

A comparison is made in the treatment of suppurative otitis media between a group using penicillin and a control group. Two thirds of the patients had scarlatinal otitis. The series comprised 266 patients, with a total of 385 affected ears. Penicillin was given "discontinuously," e. g., in small frequent doses of 15,000 units every four hours. In all cases bacterial cultures were grown. In order of frequency the bacteria demonstrated or cultured were hemolytic streptococci, pneumococci and the nonhemolytic streptococci. In the penicillin-treated group, Streptococcus could not be recovered after one day. In the nonpenicillin-treated group the streptococci could still be recovered from the aural discharge at the end of 20 days.

There was a striking difference, as well, in the length of the period that discharge from the ear continued. In treated scarlatinal patients whose ears were discharging, the average period was 6.5 days; in the nontreated patients the average was 36.5 days. Only 3.5 per cent of the penicillin-treated group required mastoid surgery. In the nonpenicillin-treated group 30.5 per cent required mastoid surgery.

The authors conclude that discontinuous penicillin therapy gives excellent results in the treatment of suppurative otitis in children.

LEWY, Chicago.

Pharynx

THE OTOLARYNGOLOGIST LOOKS AT THE TONSIL AND ADENOID PROBLEM. F. L. LEDERER and A. A. GROSSMAN, Eye, Ear, Nose & Throat Monthly **28**:577 (Dec.) 1949.

Lederer and Grossman review the subject of tonsils and adenoids. The tonsils should not be considered a useless apparatus better "out" than "in" and should not be removed indiscriminately as a prophylactic measure. The tonsils are believed to have definite functions and to be part of the defense mechanism of the body. Accordingly, the removal of normal tonsils can prove harmful to patients, especially younger children up to 6 or 7 years of age.

The indications for tonsillectomy should be reevaluated and strengthened. The procedure should be carried out in the hospital and not in the physician's office or the patient's home. A few tonsillectomies performed by an intern, even under supervision, are insufficient to qualify him to perform this operation without adequate instruction and a complete basic training in

otolaryngology. Tonsillectomy should be considered as a major procedure; the more skilled the tonsil surgeon, the greater is his respect for this supposedly simple and minor procedure.

There was in the past an erroneous concept that large tonsils were synonymous with "infected" tonsils, and this has been especially true in the case of the school child sent home because of enlarged tonsils with the recommendation that they be removed. The history is a more valuable guide than clinical examination of the tonsils. In the young child, tonsillectomy should not be performed before repeated attacks of tonsillitis have occurred in order that the role of the tonsil in the development of autoimmunization not be disturbed.

Removal of tonsils and adenoids should follow adequate evidence of disease therein. Tonsillectomy should be performed for infected tonsils, especially if these structures are producing local discomfort or general disease or are interfering with general development. Adenoids should be removed if they obstruct the pharyngeal opening of the eustachian tube to prevent hearing loss or middle ear infection. Employed rationally, it can be generally accepted that irradiation is of value in the treatment of deafness resulting from lymphoid hyperplasia in the area of the eustachian tube orifices.

Some interesting and controversial facts are presented regarding the problems of poliomyelitis in relation to tonsillectomy. However controversial, it would seem that postponement of an "elective" procedure is in the public interest and to the best advantage of the physician.

JENNES, Waterbury, Conn.

A STUDY OF DELAYED BLEEDING FOLLOWING REMOVAL OF THE TONSILS AND ADENOIDS. ARTHUR J. COOMBS, Laryngoscope **60**:296 (March) 1950.

Postoperative bleeding was greatest when acetylsalicylic acid gum (aspergum®) was used, less when vitamin K was added and still less when both ascorbic acid and vitamin K were added. As acetylsalicylic acid gum was used throughout, there was no control series.

HITSCHLER, Philadelphia.

ABERRANT SALIVARY GLAND TISSUE AT THE BASE OF THE TONGUE. A. J. VADA and KENNETH SOMERS, Laryngoscope **60**:577 (June) 1950.

Only seven cases of aberrant salivary gland tissue in the tonsillar area have been reported. The case reported here is the only one associated with other developmental abnormalities.

HITSCHLER, Philadelphia.

MANAGEMENT OF UNILATERAL CLEFTS OF THE PALATE. C. W. WALDRON, Plast. & Reconstruct. Surg. **5**:322 (April) 1950.

Waldron describes the developmental growth of the parts that make up the maxilla and relates this process to the surgery of cleft palate. By the plan for carrying out the operation he seeks to avoid in young children the ultimate growth of the parts. The operation is done in successive stages, the methods for which are given in detail. The cleft in the hard palate is closed first using Waldron's technique of utilizing a vomer flap. About two weeks later the cleft lip is closed; the soft palate is repaired still later. There are drawings which illustrate the operative procedure.

SELTZER, Philadelphia.

FIBROMA OF THE PALATE. A. E. HIEBERT and H. W. BROOKS, Plast. & Reconstruct. Surg. **5**:532 (June) 1950.

Hiebert and Brooks report the uncommon finding of hard fibroma of the palate. This is a slow-growing tumor which may be either pedunculated or sessile and is covered by pale, smooth epithelium. The genesis of this growth is still a matter of question, but its symmetrical appearance has suggested that it is the result of disturbed development in the embryo. Surgical excision, alone or combined with use of the electrocautery, is recommended by the authors. The article is well illustrated with photographs.

SELTZER, Philadelphia.

Larynx

SURGICAL TREATMENT OF BILATERAL ABDUCTOR PARALYSIS OF THE LARYNX. JOHN H. BARRETT, Ann. Otol., Rhin. & Laryng. **59**:112 (March) 1950.

On patients having bilateral abductor paralysis of the larynx following thyroidectomy, Barrett performs arytenoidectomy through a horizontal incision in the previous thyroidectomy scar. Adequate exposure is afforded, and much less postoperative disfigurement results.

Following the techniques of Woodman, the inferior cornu of the thyroid cartilage is disarticulated from the cricoid cartilage, permitting medial and upward rotation of the larynx. The cricoarytenoid joint can be palpated easily, and the arytenoid cartilage is removed by subperichrondrial dissection. The Kelly technique then is employed, whereby a linen suture placed in the thyroarytenoid muscle is transfixed through the lamina of the thyroid cartilage to give proper abduction of the vocal cord. This method eliminates the difficulty of working through a small window in the thyroid cartilage and preserves the thyroid ala to serve as an anchoring base for the vocal cord.

Two cases are reported in detail.

STEELE, Kansas City, Kan.

SMOKER'S LARYNX: A CLINICAL PATHOLOGICAL ENTITY. MERVIN C. MYERSON, Ann. Otol., Rhin. & Laryng. **59**:541 (June) 1950.

One hundred and forty-three patients with edematous fibroma of the vocal cord attributable to excessive smoking were treated by Myerson.

The clinical manifestations of this lesion are hoarseness of varying degree and vocal fatigue. While laryngeal obstruction requiring tracheotomy occurs rarely, Myerson reports one instance in this series.

The size and shape of edematous fibroma vary with the duration of the lesion and intensity of exposure to the irritants in tobacco smoke. The tumor is benign and sessile and resembles a polyp on clinical examination. It must be differentiated from localized tuberculous edematous infiltration of the vocal cord. While early lesions usually are unilateral, continued smoking tends to produce similar changes in the uninvolved cord.

Histologic sections of the lesion show nodules composed of fibrous connective tissue in an edematous stroma. In certain areas there is inflammatory cell infiltration. Eosinophils are not seen. Hyalinized collagen occurs in the stroma in cases of long standing. The epithelium usually is stratified.

Treatment of the disease is by indirect laryngoscopic forceps removal of the cordal lesions, according to the author. Only the early cases are amenable to conservative or nonsurgical treatment. The practice of prescribing vocal rest for two or more weeks is based on a faulty conception of the disease, for if the lesion does not disappear within 24 hours, it may safely be considered permanent.

STEELE, Kansas City, Kan.

PAPILLOMA OF THE LARYNX: A REVIEW OF 109 CASES WITH A PRELIMINARY REPORT OF AUREOMYCIN THERAPY. PAUL H. HOLINGER, KENNETH C. JOHNSTON and GEORGE C. ANISON, Ann. Otol., Rhin. & Laryng. **59**:547 (June) 1950.

Three possible etiological factors in laryngeal papilloma are a chronic irritation, hormonal agent and filtrable virus. Similar lesions elsewhere on the body, such as plantar warts, apparently caused by local irritation, tend to support the irritation theory. Frequent spontaneous disappearance of papillomatous lesions at puberty, the absence of lesions in one of the authors' patients during each of three pregnancies with recurrence when menstruation resumed and the reported response to topical application of an estrogenic substance (amniotin® in oil) support the hormonal theory. The transferability of the growth by a filtrable agent and the response of seven children reported in this series to aureomycin therapy give support to the theory of viral origin.

A series of 109 cases of papilloma of the larynx is presented. In the group of 54 patients below 16 years of age in whom symptoms developed, 44 (81 per cent) were found to have multiple papillomas, while 10 (19 per cent)showed single papillomas. In 55 patients in whom symptoms developed during adult life, the papillomas were multiple in 20 (36 per cent) and single in 35 (64 per cent).

Most of the patients were treated by repeated direct laryngoscopic forceps removal of the papillomas. Tracheotomy was performed in 16 children and three adults. Cautery was used only occasionally. Podophyllum resin (podophyllin®) was applied topically in two cases, but appeared to cause proliferation of the growth. X-ray therapy was used in one adult patient because of frequent recurrence not controlled by forceps removal.

A preliminary report is made of the seven children who were given aureomycin after forceps removal of papilloma. The dose administered was 25 to 50 mg. per kilogram body weight per day in divided doses for 14 to 21 days. In three instances, a second course of therapy was given. The optimum dose, duration of treatment and interval between courses of aureomycin have not been apparent from observation of this series. However, it would appear that a dose of 50 mg. per kilogram body weight per day seems indicated, with treatment carried out for at least 21 days. While it is emphasized that this form of treatment was used only as an adjunct to forceps removal, it was noted that patients who obtained a good result showed smoother mucosal surfaces than those patients in whom forceps removal had been used alone.

The authors state that aureomycin may be useful in the treatment of papilloma of the larynx, although the length of time since the institution of treatment in the series is too brief to allow for final conclusions.

STEELE, Kansas City, Kan.

SURGICAL TREATMENT OF CANCER OF THE LARYNX. JUSTO M. ALONSO, Rev. otorrhinolaring. **9**:12 2(Dec.) 1949.

Alonso points out that in surgery of the larynx three basic principles are to be followed: (1) to save the patient's life; (2) if possible, to preserve the function of the larynx, and (3) when the disease is too extensive, to relieve the suffering of the patient.

No one technique of surgery can be applied in every case of cancer of the larynx. Alonso describes his own technique depending on the site and extent of the disease. If it is limited to the pyriform sinus, he does a "partial vertical laryngectomy" and always leaves a lateral pharyngeal opening. Two or three months after the operation, he closes the opening by plastic surgery. If the disease involves the vestibule of the larynx, he performs a "partial horizontal laryngectomy." This is done with the purpose of preserving phonation; and finally in cases in which the tumors involve the subglottic region, he does a "partial anterior tracheotomy." This is particularly valuable when the growth involves the anterior portion of the subglottic space or in small tumors which have not involved either the anterior commissure or the vocal cords. Actually the latter procedure is used infrequently.

PERSKY, Philadelphia.

Nose

A METHOD FOR REMOVAL OF PEDUNCULATED NASOPHARYNGEAL POLYPUS. R. T. UHLS, Eye, Ear, Nose & Throat Monthly **29**:139 (March) 1950.

Uhls describes a method for removal of giant pedunculated nasopharyngeal polyps to be utilized when it is impossible to engage the polyp by manipulation of a snare introduced through the nose. A rubber catheter is introduced into the nostril, slid past the polyp and brought out through the mouth. The ends of a long loop of snare wire are pushed through the eye of the catheter and bent to prevent injury to the mucous membrane when drawn into the nose. The snare wire is then drawn into the mouth and out through the nose, leaving the loop in the desired position below the tumor. It is an easy matter to manipulate the wire up behind the polypus. The wire is then seized by a curved hemostat and carried up behind the polypus.

The snare, which must be without a stylus, is threaded with the snare wire while *in situ* and the cannula pushed into the nose, back against the polypus. The snare wire should be just long enough to slip under, then over, the growth. The growth is grasped with a tenaculum, cut with the snare and delivered through the mouth.

JENNES, Waterbury, Conn.

SURGICAL TREATMENT OF THE BIFID NOSE. J. P. WEBSTER and E. G. DEMING, Plast. & Reconstruct. Surg. **6**:1 (July) 1950.

Webster and Deming discuss in detail the surgical treatment of the bifid nose. The summary of the entire article presents an excellent and well described procedure. A general analysis of bifid nose and concomitant deformities is made on the basis of 10 patients who came under their care in the clinic during the past 18 years. These 10 cases are presented, together with the experience gained from the eight patients who underwent surgery. Procedures for the correction of this deformity are described together with various modifications. Other authors have been of the opinion that the problem of hypertelorism was insurmountable. However, the importance of reduction in the wide spacing of the component parts of the face adjacent to the eyes to produce an optical illusion minimizing the appearance of hypertelorism was realized and is here presented as a fundamental factor in giving patients with either true or suggested hypertelorism as normal an appearance as possible. This is accomplished by the excision of tissue in the midline of the forehead and bridge of the nose with closure after wide lateral undermining, possibly supplemented with Y-V plastic procedures of the eyebrows. The wide nose is narrowed by fracture of the nasal processes with medical displacement. Further elimination of epicanthal folds and narrowing of the space between the inner canthi is accomplished by the use of free grafts of cartilage or excess nasal bone to build up the bridge. Because of the frequent development of personality complexes, surgical correction of the bifid nose should be started at an early age. There are 34 excellent illustrations of 10 cases.

SELTZER, Philadelphia.

MALIGNANCY OF THE NASAL SINUSES. W. RAYMOND MCKENZIE, South. M. J. **41**:156 (Feb.) 1948.

McKenzie states that malignant disease of the nasal accessory sinuses occurs frequently enough to demand that it be kept in mind. It recognizes no social or racial barriers or age or condition. An early diagnosis is not difficult to make if the possibility of malignancy is kept in mind. Because of the accessibility of the nose to direct inspection, examination by anterior and posterior rhinoscopy, nasopharyngoscopy, transillumination, x-ray and taking of biopsy, the diagnosis of malignant disease could and should be made earlier than it is at the present time. The maxillary and ethmoidal sinuses are the ones most often involved; almost all types of growths occur. The disease may occur in the young but not so frequently as it occurs in older patients. The early symptoms are insidious, beginning with a unilateral nasal stuffiness and unilateral discharge, at first watery or mucoid, later becoming blood tinged or bloody. Localized pain, headache and loss of the sense of smell are also symptoms of the disease. In making an examination, one should look for nasal obstruction, complete or partial; blood-stained discharge, and a growth which usually bleeds easily. The growth may be rough or smooth, soft or hard, pedunculated and freely movable or sessile and fixed. Such a growth should always be removed for biopsy studies. Nasal smears and cultures, a complete blood examination, especially the sedimentation time, and careful x-ray examination of the sinuses should be carried out.

The prognosis of malignant disease of the sinuses depends on a number of factors, such as the age and general condition of the patient, whether or not the condition is operable, the presence or absence of such concomitant conditions as heart or kidney disease, the location of the lesion, the stage of its development and the character of the growth.

SINGLETON, Dallas, Texas.

BACTERIOLOGICAL EXAMINATIONS IN MAXILLARY SINUSITIS. TORSTEN BJÖRKWALL, Acta oto-laryng., 1950, supp. 83, p. 1.

Bacteriological studies of the maxillary sinus were made with the purpose of determining the following: the nature of the normal bacterial flora of the nasal cavity and the antrum; which bacteria are causative organisms in clinically different infection reactions of the sinuses; whether or not it is possible to ascertain inflammation of the maxillary sinus on the basis of the flora of the nasal cavity itself, and whether or not the nature of the flora of the nasal meatus and the maxillary sinus gives information as to the prognosis of the sinusitis and indications for surgical intervention.

The series reported covers 115 persons whose antrums were examined 288 times. The nasal cavities were examined all but 12 of these times. There were 22 control subjects who gave negative reactions on puncture, x-ray examination and diaphanoscopy. These subjects had free air passages between the sinus and the nasal cavity proper.

In 70 per cent of the patients with healthy noses the flora was composed of Staphylococcus albus and Corynebacterium, either in combination or separately. This is considered, therefore, the normal flora. A mixed culture of this flora and pathogenic bacteria occurred in 15 per cent of all patients, and a pure culture of pathogenic flora occurred in 15 per cent. In mucous sinusitis, however, normal flora was found in 50 per cent of the patients. Mixed infection occurred in 33 per cent and a pure culture of pathogenic bacteria in 17 per cent.

In purulent sinusitis, normal flora was found in the nasal meatus in only 8 per cent of the patients. Mixed infection containing the pathogenic bacteria was found in 61 per cent. There was a pure culture of pathogenic bacteria in 31 per cent. Thus it will be observed that pathogenic bacteria were found in the meatuses of 92 per cent of the patients involved. Streptococcus occurred in 35 per cent, pneumococcus in 29 per cent and Staphylococcus aureus in 20 per cent. Escherichia coli and its similar relatives were found in 35 per cent.

In surgically treated patients there was a normal flora in 6 per cent. There was a mixed culture in 58 per cent and a pure culture of pathogens in 36 per cent. When a sinus was healing there was a shift from the pathogenic to the normal flora. The flora of the healthy half of a nasal meatus usually resembles the bacterial flora of mucous sinusitis.

Half of a group of 96 patients with purulent sinusitis were surgically treated. Of this group, 63 per cent showed pure cultures. In a series of 17 in which there was foul-smelling pus there were pure cultures in 47 per cent. No special bacteria to which the bad odor could be ascribed were found. Repeated examination of the bacterial flora in the same sinus revealed constancy of result on culture. A pathogenic bacterium was not found to oust an organism.

A healthy maxillary antrum is sterile. In purulent maxillary sinusitis normal flora of the nasal meatus is found in only a minority of instances. Most of these show pathogenic bacteria in a mixed or a pure culture. In foul-smelling pus many of the organisms are facultative anaerobes.

The results indicated that the prognosis of healing without surgery was worst in cases caused by streptococci. If the Corynebacterium is not found on antral culture in maxillary disease it is probable that the possibilities of healing without surgery are small. Conversely, however, when normal flora (Staphylococcus albus and/or Corynebacterium) is found to be present during the course of treatment, healing may be anticipated and surgery should be postponed.

ROBERT LEWY, Chicago.

Miscellaneous

RATIONAL THERAPY FOR COMMON COLDS AND NASOSINUSITIS. MAX UNGER, New York State J. Med. **50**:295 (Feb. 1) 1950.

Unger states that the sulfonamides and penicillin have been disappointing in the treatment of nasal conditions. A study of both normal and pathological anatomy and of the physiology of the nasal mucous membrane has helped him to establish this opinion. During a cold secretion from the nose is increased to from 4,000 to 5,000 cc. in 24 hours. Weighing patients at the beginning and at the end of a cold shows a weight loss of from 2 to 5 pounds (0.9 to

2.3 Kg.) in spite of fluid intake (water and fruit juices). The vasoconstrictors diminish the serum and phagocytes and are a direct hindrance to mucosal defense against germs. One should reenforce nature in helping to remove the products of inflammation. This is best accomplished by using copious amounts of isotonic sodium chloride solution. A good way to gage the "sittings" is to follow the sneezing attacks, for sneezing indicates that undesirable irritants are being expelled. One may irrigate the nose every hour if necessary. Six or seven irrigations during the first twelve hours after the onset will give the patient much comfort and enable him to sleep without sedatives. Unger thinks that the attempt to sterilize the nose by antiseptics is futile. Irrigations as here outlined will shorten the duration of a cold and have few if any sequelae. Three photomicrographs serve to illustrate the author's views.

VOORHEES, New York.

EMERGENCY THERAPEUTIC BRONCHOSCOPY IN THE CRITICALLY ILL ASTHMATIC. HARRY MARKOW, New York J. Med. **50**:549 (March 1) 1950.

Having worked in the Division of Immunology at Beth-El Hospital, New York, Markow discusses briefly the chronic type of asthma. Patients with chronic asthma become epinephrine-fast and fail to respond to every known remedy commonly tried. They become cyanotic in spite of administration of oxygen, have a pulse rate of 150 and die from asphyxia. Autopsy shows masses of tough mucus which completely block the bronchial tree. Dehydration is an important factor in the sticky composition of this exudate. A case is reported at length in which the patient had all the above symptoms and on whom bronchoscsopy was performed while the patient was moribund. After 10 weeks in the hospital the patient reported that he was well and had no further attacks of asthma. Markow states: "Asphyxiation due to bronchial obstruction is a major cause of death in bronchial asthma. In former years one used to speak of the patient drowning in his own secretions. This is still an accurate observation in status asthmaticus."

In summary, a case is reported of a moribund patient whose life was saved by a timely bronchoscopy with removal of the sticky secretion which acted as a foreign body. The bronchoscopist hesitates to put the tube into a dying patient, and yet he must do this to save life. There is everything to gain and nothing to lose. It is possible that some forms of medication actually jeopardize life by helping to produce the obstructive tenacious secretion; just how this comes about is problematical, but how to prevent a catastrophe is a question which bronchoscopy may answer.

VOORHEES, New York.

THE MANAGEMENT OF LYE BURNS OF THE ESOPHAGUS. GILBERT E. FISHER and JAMES J. HICKS, South. M. J. **41**:591 (July) 1948.

Fisher and Hicks report having treated 34 patients for lye burns of the esophagus in the past year. Immediately after the patient presents himself in the emergency room for treatment, he is given a mouth wash of a weak solution of acetic acid and is asked to swallow a small amount of it. This treatment is followed by a mouth wash and the swallowing of a bland oil. A nasal tube is then passed into the stomach, and the stomach is washed thoroughly with diluted acetic acid and water. A bland oil is then instilled into the stomach. The tube is left in place for three days, and a high caloric, high vitamin diet is administered. On the fourth day the patient is examined with an esophagoscope. If only small areas of the esophagus are burned, daily dilatations are begun with a rubber bougie. The size of the bougie varies with the size and age of the patient. After 10 or 12 dilatations these patients usually need no further treatment. In the severer cases in which burns occur at different levels and involve the entire circumference of the esophagus, daily dilatations are done using the E. N. Broyles esophageal dilatators as tolerated; they vary in size from 12 to 32 French. If the dilatation can be carried out successfully at the beginning the patient is at once directed to remain on a liquid or semisolid diet. These patients must be seen daily for at least two weeks to see that they are receiving sufficient food and fluids and to see that swallowing is not impaired.

Greatest difficulty occurs in those patients who are not seen until several days after receiving the burn. In these patients esophagoscopy must be carried out at once to determine the extent of mucosal damage. In severe burns involving the hypopharynx and the upper one third of the

esophagus, dilatation is very difficult. These patients should have dilatation treatment daily or every other day, with the largest dilatator possible but with care not to overstretch the injured tissue. If after a few days a 24 French dilatator can be tolerated and frequent dilatations are maintained for a month or longer, the interval may be diminished to twice weekly, and this should be continued over a much longer time. If the dilatations are discontinued, complete stenosis may follow. When this occurs an intrathoracic esophagogastrostomy may have to be done. If the stenosis is not complete, weekly or biweekly dilatations will usually suffice. These patients may have some difficulty during periods of acute infection of the upper respiratory tract. Seven illustrative cases are presented.

SINGLETON, Dallas, Texas.

THE TREATMENT OF BELL'S PALSY WITH HISTAMINE. D. A. SKINNER, Ann. Otol., Rhin. & Laryng. **59**:197 (March) 1950.

Skinner treated 19 patients with Bell's palsy (neuropathy of facial nerve due to pressure) by administering histamine diphosphate by subcutaneous injection every two or three days.

In 17 patients "low dose" therapy was utilized, starting with 0.1 cc. of a 1 : 10,000,000 dilution and gradually increasing until the optimum effective dose was reached. When improvement occurred, the dose was maintained at that level.

"High dose" therapy was employed in two patients, starting with 0.1 cc. of 1 : 10,000 dilution and gradually increasing to 1.0 cc. of 1 : 10,000 dilution. In these patients improvement did not occur before one month of treatment. More rapid response was effected by using the low dose type of therapy.

In 16 patients, or 84 per cent, the rapidity of improvement was phenomenal. In this group the shortest recovery occurred in four days, the longest in 48 days and the average in 19 days. The paralysis recurred in two patients when the dose was increased above the optimum effective amount, but restoration took place when the proper effective dose again was given. In one patient paralysis did not recur when the dose was increased far above the optimum effective amount. In another completely recovered patient, the administration of 50 mg. of tripelennamine (pyribenzamine®) hydrochloride caused a slight recurrence of paralysis.

Skinner advocates the additional use of liquid petrolatum eye drops, hot compresses and massage of the facial muscles, facial splints or strapping of the face with cellulose tape and elimination of foci of infection. In patients failing to show early improvement, electrical stimulation is of value.

STEELE, Kansas City, Kan.

Directory of Otolaryngological Societies *

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President: Dr. Jose Gros. Information may be secured from Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40.

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NATIONAL

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Place: Cleveland. Time: Jan. 15, 1951.
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HEARING COUNSELING SERVICE to help your patient understand his hearing problem and to help in the selection of a hearing aid if one is advisable.

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No one knows better than you that hard-of-hearing patients are sensitive about their hearing defects. No one knows better that many a patient refuses to buy a much-needed hearing aid, that many an instrument is unused, hidden away in a drawer or shoved back on a shelf.

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The Sonotone technician training program is directed by recognized acoustic engineers to give *intelligent* assistance to the doctor and his hard-of-hearing patients.

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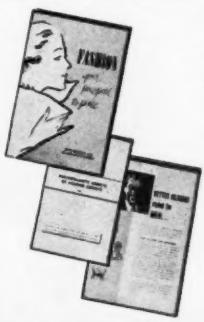

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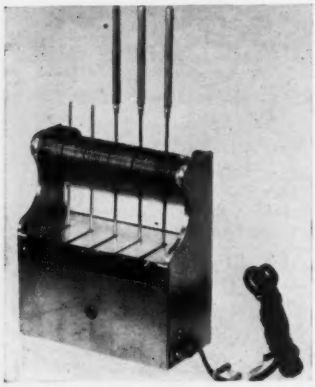

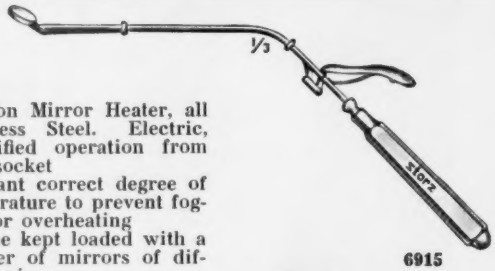

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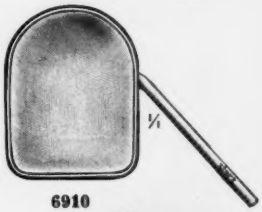

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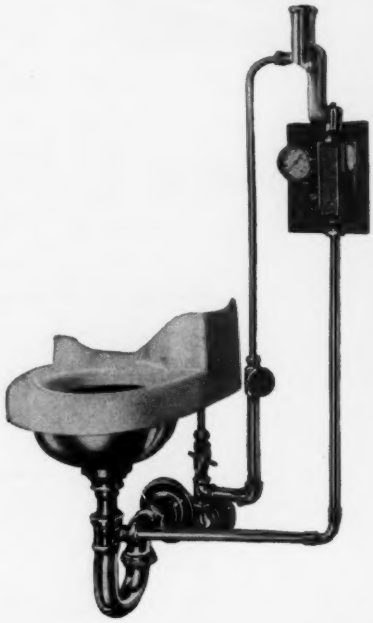

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Archives of Otolaryngology, March, 1947: 294-297
Bulletin of the Johns Hopkins Hospital, Sept., 1948: 225-228
The Eye, Ear, Nose & Throat Monthly, April, 1950: 200-203
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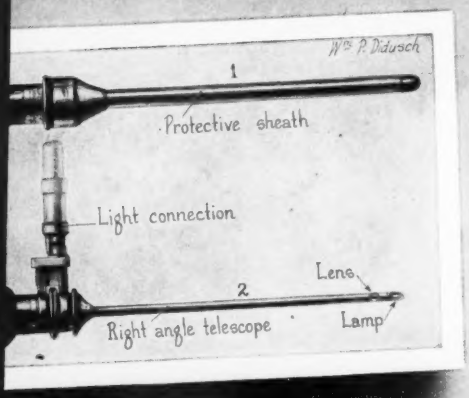

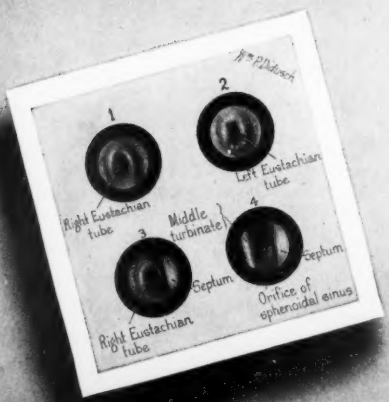

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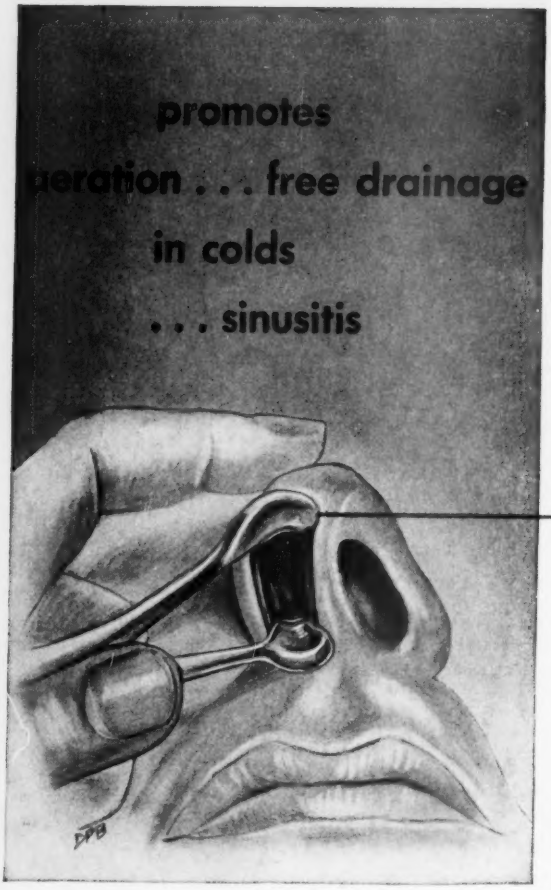
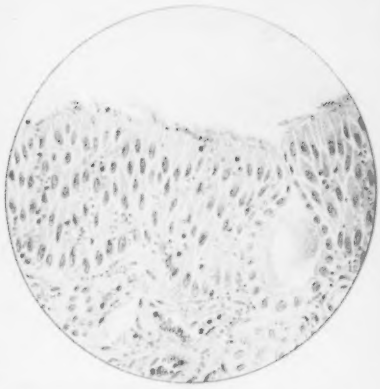
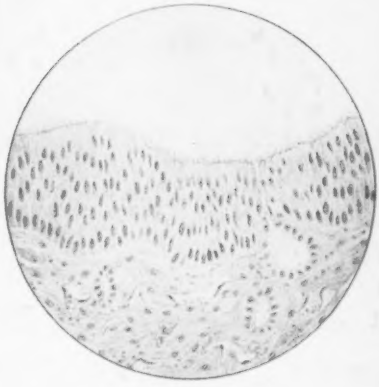




Nasal membrane showing increased leukocytes with denudation of cilia.

Normal appearing nasal epithelium.



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